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Epidemiological Notes on Some Tropical Mycoses.

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GENERAL REMARKS.

Diseases due to fungi have, since the days of Virchow, been called mycoses. They are separated into two large groups: (1) internal mycoses (internal diseases due to fungi), and (2) external mycoses or dermatomycoses (skin diseases due to fungi).

Fungi, from a practical point of view, may be defined as vegetal organisms of higher development than bacteria, from which they differ principally in the following two points: (*a*) they are of larger dimensions, (*b*) they always reproduce by spores, never by fission. Of course, *natura non facit saltus*, and intermediate organisms are found, the assignation of which to the fungi or to the bacteria is difficult to determine. This is not the place to enter into any details concerning the classification of fungi; it may be mentioned, however, that from a practical standpoint two groups may be distinguished: the *yeasts* or *budding fungi* and the *filamentous fungi*. The filamentous fungi may be further subdivided into (*a*) filamentous fungi with thin, almost bacillary mycelium, and (*b*) filamentous fungi with large mycelium.

Some pathogenic fungi seem to have a limited geographical distribution, others a cosmopolitan one. It would appear that climatic conditions have a great influence on many fungi; some die in a temperate climate, others lose their pathogenicity. Cultures of *Cladosporium mansoni* often die out in a temperate climate. Cultures of *Endodermophytons*, the fungi which cause tokelau or tinea imbricata, are frequently not capable of reproducing the disease in Europe.

Fungi are capable of producing disease in plants and animals. In plants they may cause terrible epidemics—it is sufficient to quote the fungal disease (due to *Hemileia vastatrix*) which within three years destroyed all the coffee plantations in Ceylon. In animals, including man, fungi produce a number of important diseases, but seldom, if ever, give rise to true epidemics. Epidemic diseases in animals are usually of bacterial origin.

Tropical mycoses.—Tropical mycoses are mycoses occurring only in the tropics, or much more common in the tropical than in the temperate zones. Like mycoses in general, they may be separated into two groups—internal tropical mycoses and external tropical mycoses.

With regard to internal tropical mycoses, I will touch on only two conditions: tonsillomycoses and bronchomycoses.

Tonsillomycoses.—This term is used to denote any fungal disease of the tonsils. The more important ones are the following: (*a*) tonsillomycosis membranacea or

diphtheriasimilis; (*b*) tonsillomycosis follicularis; (*c*) tonsillomycosis spinulosa; (*d*) tonsilloactinomycosis; (*e*) tonsillopseudoactinomycosis.

From an epidemiological point of view, the most interesting is probably tonsillomycosis membranacea, since it may clinically closely resemble diphtheria.

Clinical.—The onset is often sudden, with a severe sore throat and difficulty in swallowing; the patient looks and feels ill, and complains of great prostration and sometimes of rheumatoid pains in the joints; fever is present and may be fairly high (102° to 103° F.). Some of the cervical glands may be swollen and tender. Inspection of the throat will show cream-white patches on the tonsils, the uvula and, occasionally, the soft palate; the patches often coalesce. Removal of portions of these patches is often easy, and in some cases leaves a very slightly ulcerated bleeding surface. If the membrane-like structure is placed between two slides, it often feels like putty, and lacks the elasticity and resiliency of a diphtheritic pseudo-membrane.

Diagnosis is based on the microscopical and cultural examination of the white patches, which usually reveal a large number of fungal elements, generally in the form of yeast-like bodies. The condition is differentiated from diphtheria by the presence of the fungus and absence of the diphtheria bacillus. It must be borne in mind, however, that cases of mixed infection—diphtheria *plus* mycosis—are occasionally met with.

The condition must be differentiated from Plaut-Vincent's angina; in mycosis spirochætes are absent or exceedingly rare. Moreover, in Plaut-Vincent's angina, if the white exudate—which is usually a dirty greyish colour rather than cream-white—is removed, an ulcer is seen, frequently fairly deep, while in mycosis the removal of mycotic membrane will ordinarily show only very superficial lesions.

The prognosis is generally, but not invariably, favourable. In a case in Ceylon the fungal infection spread to the bronchi and lungs, and a severe mycotic broncho-pneumonia developed, with a fatal end.

Illustrative Cases.

Case 1.—A Singhalese girl, aged about 11, was admitted to the Infectious Diseases Hospital, Colombo, in 1910, with the diagnosis of diphtheria. There were white patches on the tonsils, uvula and soft palate. The temperature was rather high (102° F.); the pulse was rapid and of low pressure. There was some swelling at the angle of the jaw. The child developed symptoms of broncho-pneumonia and died three days after admission. Anti-diphtheritic serum was given twice by the physician in charge of the hospital before I was called in to see the patient. The microscopical and bacteriological examination of the patches for the Klebs-Löffler bacillus, carried out with the usual technique, serum media, etc, remained negative. Instead, numerous yeast-like and filamentous elements were seen in the preparation, and in the inoculated culture media numerous colonies of monilia developed which further investigation showed to be *Monilia tropicalis*.

Case 2.—On August 5, 1921, Pensioner N. (Ministry of Pensions Hospital, Orpington), developed tonsillitis, with temperature 102° F., a rapid pulse-rate and prostration. Inspection of the throat showed a white membrane on the tonsils and fauces. It was easily detachable, but rapidly re-formed. Neither in the direct smear nor by culture methods were diphtheria bacilli found. In the direct smear, made at the bedside, were a large number of monilia. From cultures on Löffler's medium and glucose agar, monilia was grown at 37° C. and isolated in pure culture. It turned out to be *Monilia metalondinensis* Castellani, producing gas in glucose, lævulose, maltose and galactose. The patient made a good recovery after using a chlorine gargle.

Epidemiological remarks.—With regard to ætiology, the condition is caused by fungi, generally of the genus Monilia. The attack not rarely begins apparently after a chill. The condition is more frequent in the tropics than in the temperate zones, but cases have been observed by myself and others in this country. Children and adults, males and females, may be affected; it seems to be rare in old people. As a rule, only sporadic cases are seen. Occasionally, two or three cases may occur in

the same institution, but the disease never takes on a truly epidemic character. How do these cases arise? It must be remembered that a great many apparently healthy individuals are monilia-carriers, that is to say, monilia fungi are found in their mouths—in the saliva, and, not infrequently, in the crypts of the tonsils. It is possible that a chill may make these fungi capable of producing disease by lowering the natural resistance of the tissues. It is possible also that certain bacteria, principally streptococci, may produce a superficial inflammation of the mucosa and that the fungus finds in the damaged mucosa a favourable soil for development. When several cases occur in the same institution, it may be that a virulent strain is transmitted from one individual to another by direct contact, or more usually, indirect contact by means of spoons, cups, tumblers, etc., nor should one for get droplet infection.

Bronchomycoses.—The term bronchomycosis is used to cover any disease of the bronchi and lungs caused by fungi. The bronchomycoses may be separated into the following groups:—

(1) Due to fungi which are either yeasts or appear like yeasts in the lesions and tissues, viz., round or oval cells, at times budding—"blastomycoses."

(2) Due to filamentous fungi, with thin bacillus-like mycelium (Nocardiaceæ)—"bronchonocardiases."

(3) Due to fila mentous fungi of larger size, such as Aspergillus, Penicillium, etc., —"aspergillosis," "penicilliosis," etc.

Whatever the causative fungus, in a number of cases the condition resembles, clinically, pulmonary tuberculosis, the patient losing flesh, having fever, feeling very weak; there is mucopurulent expectoration, at times containing blood and occasionally true hæmoptysis develops. The course is usually prolonged and the disease often terminates in death unless the correct diagnosis is made in time and the appropriate treatment given. Bronchomycoses do not occur in epidemic form, only sporadically.

With regard to the portal of entry, there are probably two ways: by inhalation of spores, or by abrasions of the skin. In the latter case, some skin lesions generally develop and the bronchomycosis is, in reality, secondary to the disease of the skin. This is often the case in American blastomycosis.

I will devote a few words to a tropical condition which, in all probability, is a form of bronchomycosis—namely, "tea-taster's cough" or "tea-factory cough."

In 1906 a young assistant in one of the big Ceylon firms, a tea-taster, came to consult me about a chronic cough, which, he said, had not yielded to ordinary treatment, and had been suspected by several medical men to be of tuberculous origin. He emphatically stated, however, that he did not believe the condition was tuberculosis. "I am merely suffering," he said, "from tea-taster's cough," an expression I had never heard before. The general condition of the patient was good, and physical examination of the chest revealed only a few coarse râles. The microscopical examination of the sputum was negative for tuberculosis; on the other hand, I noticed, microscopically, some mycelial filaments and some yeast-like bodies. I inoculated several glucose agar tubes and grew a monilia fungus which, at the time, I believed to be an endomyces.

How did this patient become infected? Tea-tasters, in order to judge of the quality of the various teas, not only taste infusions, but also often fill their hands with the tea leaves and bury their noses in them, sniffing them up; in this way a certain amount of tea dust enters the nasal cavities.

Now, if one examines tea dust in Ceylon, one finds that it contains fungi of the genus *Monilia* constantly, of the genera *Aspergillus* and *Penicillium* frequently, and of the genus *Oidium* (*Geotricum*, *Mycoderma*) occasionally. A peculiar streptococcus is also often present. The same organisms are not rarely found in the nasal cavities of tea-tasters, and when bronchial symptoms appear in them, monilia-like fungi

are present in the expectoration. It is probable, therefore, that the so-called tea-taster's cough is a mycosis, especially since a guinea-pig in the nostrils of which I insufflated tea-dust regularly for several weeks, died with symptoms of chronic monilial broncho-pneumonia, and at the post-mortem examination monilia fungi were grown from the lungs.

What I have said about " tea-taster's cough " applies to a great extent to the so-called " tea factory cough." For many years, planters in Ceylon have noted that the coolies doing work in tea factories, where the leaves are dried and there is a large amount of tea dust floating about, after some months become weak, lose flesh and often have a cough with mucopurulent expectoration. The planters have found by experience that the coolies must be taken away from the factory and sent to work in the field, when the symptoms slowly disappear. In Ceylon, I examined some of the coolies and their expectoration practically always contained fungi of the genus *Monilia*, and at times other fungi.

Tropical external mycoses (tropical dermatomycoses).—Tropical external mycoses, or tropical skin diseases due to fungi, are common and it is impossible to deal with all, or even a majority during the time allotted to me. I shall, therefore, confine my remarks to those on which I have carried out personal investigations.

Madura Foot (Mycetoma).

Clinical.—In a typical case, the whole foot is swollen and the surface studded with nodules and sinuses from which exudes pus, containing grains of various colours—white, yellow, black, red. The course is chronic and, except at the very beginning, no treatment is of any avail except amputation.

Epidemiology.—The condition is common in Southern India, especially in the countryside around the town of Madura, but never takes an epidemic course.

With regard to climatology, the disease is extremely rare in the temperate zone; a few cases have been reported, however, from Italy, Spain, France, the Balkans, North America and the Argentine. It is interesting to note that apparently it does not occur in Northern Australia, although that portion of the Australian Continent may be considered to be tropical.

The condition is more common in males than in females; it is seldom seen in children or in old people. It is mostly found in farmers and farm labourers, who go bare-footed.

Ætiology.—Mycetoma, which is a fairly well defined clinical entity, may be caused by the most diverse fungi, belonging to different classes, orders, families, genera and species. Since Chalmers's and Archibald's work on the ætiology of mycetoma, it is usual to separate the condition into two ætiological types: actinomycetoma (mycetoma actinomyceticum, actinomycosis) and maduromycetoma (mycetoma maduromyceticum, maduromycosis). The principal feature of mycetoma of both types is the presence of grains which are, in reality, fungal sclerotia. These grains in actinomycetoma are composed of fine non-segmented mycelial filaments—usually not exceeding 1 micron in diameter—in which ordinarily the walls are not clearly differentiated from the contents and in which chlamydospores are absent. These fungi belong to the genera *Nocardia* Toni and Trevisan, 1889 (Actinomyces) and *Cohnistreptothrix* Pinoy, 1911; family Nocardiaceæ Castellani and Chalmers, 1918; order Microsiphonales Vuillemin, 1912; sub-class Hyphales Vuillemin, 1912; class Fungi imperfecti Fuckel, 1869.

In mycetoma maduromyceticum (maduromycetoma, maduromycosis) the grains are composed of large segmented mycelial filaments with well-defined walls and, usually, chlamydospores. These fungi belong to the most different botanical groups. Fungi of the following genera have been found: *Madurella* Brumpt, 1905, and *Indiella* Brumpt, 1906, belonging to the sub-order Arthrosporineæ, order Thallosporales; *Glenospora* Berkeley and Curtis, 1876, belonging to the sub-order Aleurio-

porineæ, order Conidiosporales; *Scedosporium* Saccardo, belonging to the sub-order Sporophorineæ, order Conidiosporales; genera *Allescheria* Saccardo; *Aspergillus* Micheli, 1925; *Sterigmatocystis* Cramer; *Penicillium* Link, 1809, belonging to the class Ascomycetes.

The causal fungus is introduced into some part of the body, generally the foot, by means of a splinter of bamboo or some other wood, a sharp stone, a knife, etc.

Dhobie's Itch (Tinea Cruris).

Clinical.—In typical cases, this mycotic infection affects chiefly the cruro-inguinal region. Large patches are seen with a festooned appearance and raised abrupt margin. The pruritus is intense.

Epidemiological.—The condition is extremely common all over the tropics and subtropics, where it goes by several local names, such as Burma itch, Hong-kong itch. It must be noted, however, that it is found also in the temperate zone, and it is not at all rare in this country, where epidemics of it in schools are fairly frequent in the summer.

Mycology.—Several different fungi may cause dhobie's itch; the two commonest ones are *Epidermophyton cruris* and *Epidermophyton rubrum*, described by me some years ago. The first fungus is characterized by its colonies on glucose agar being a canary yellowish colour, the second type by the colonies being red.

Communicability.—The disease is very contagious; it may spread by direct contact as when the wife is infected by the husband, but usually we are dealing with indirect contagion by means of towels, sponges and bathroom appliances. Tinea cruris is known in the East as dhobie's itch, from the popular belief that it is contracted from linen which has been contaminated while being washed by the dhobie (native laundryman). Whether this belief is well founded, I cannot say. I have never succeeded in finding the fungus in clothes newly received from the dhobie, either microscopically or by inoculating small portions of the linen in sugar media. I am, however, inclined to think that the popular belief may to a certain extent be correct. In Colombo, dhobies are, or were, in the habit of washing the clothes in a lake or in small pools of water more or less stagnant. It is certain that clothes belonging to infected persons are washed together with other clothes. We have been told by old sufferers from dhobie's itch, who used to be frequently re-infected, that on their ceasing to give their clothes to the dhobie, and having them washed in the house instead, the disease did not again affect them.

Tinea Flava.

Clinical.—Tinea flava is characterized by the presence of large yellow patches. In coloured people these patches stand out, the colour being much lighter than the surrounding healthy skin. The yellow may be of different hues, from dark, deep orange-yellow to light canary, almost white. The patches are generally roundish or oval, smooth and sharply defined, with margins not elevated. In recent patches, however, the margin may be slightly elevated. Sometimes patches coalesce, giving rise to the diffuse form of the disease. The regions of the body most frequently affected are, in order of frequency, the face, neck, chest and abdomen. There is not, as a rule, any pruritus, except occasionally in recent patches. The patches are not desquamating, or only slightly so. Occasionally, in Ceylon and Southern India, one is surprised to see a Singhalese or Tamil native with the face, chest, neck and trunk of a much lighter colour than in the other natives. On closer examination it will be found that the apparently light colour of the skin is merely due to a light diffuse form of tinea flava.

In Ceylon, when the spots are small, and found on the face of young girls, they are considered to be beauty spots, and in Singhalese poetic literature reference is

often made to the minute, light yellow beauty spots on the face of Singhalese young women. These spots, so much admired by the natives, who have coined a special poetic expression for them (" gomera "), are, in reality, merely small patches of tinea flava.

Tinea flava may affect Europeans. The patches are yellow and similar to those found in natives, but owing to the colour of the European skin they do not stand out so vividly. It must also be noted that if the patient has taken some violent exercise, and the skin is perspiring, the patches look red instead of yellow.

Tinea flava is differentiated from the ordinary pityriasis versicolor of temperate climates because it affects the face more than any other part of the body, and is very difficult to cure. Moreover, the fungus producing it seems to have a disturbing action on pigment production, as depigmented patches often remain after the mycosis has been cured.

Epidemiological.—This mycosis is extremely common all over the tropics, especially in Southern India, Ceylon, Malaya, Java, Indo-China and China. I have found it fairly common in Central America, Honduras, the low-lying districts of Guatemala and Panama. The condition is present, in my experience, also in Louisiana. Both men and women are attacked, also children. In fact, the disease generally begins in childhood and never disappears completely unless thoroughly treated. The condition is probably spread by contact. either direct or indirect, through clothes.

Tinea Nigra.

Tinea nigra is characterized by the presence of jet-black patches caused by a fungus of the genus *Cladosporium*, which I called *Cladosporium mansoni*, in honour of Sir Patrick Manson. This fungus is fairly easily grown on sugar media, giving rise to black colonies. The condition is not rare in natives, and may be found also in Europeans, as shown by the following case:—

A European medical man went to Burmah from Ceylon for a pleasure trip. On returning to Ceylon he noticed a roundish, slightly elevated black spot on the palm of his left hand. This spot slowly increased in size for two months, becoming as large as a halfpenny piece. A single application of formaldehyde made it disappear, but three months later it reappeared, A second application of formaldehyde cured the condition permanently. Cultures were made from the patch, before treatment, and a cladosporium was isolated, identical with the fungus found in native cases.

The geographical distribution seems to be limited to tropical Asia and tropical America. No cases have been reported from Africa, Australia or Europe.

Infection probably takes place by contact, either direct or indirect.

Pinta.

Pinta is generally defined as a dermatosis characterized by patches of various colours—jet-black, bronzine black, violet, red, yellow and white—and since the investigations of Ruiz y Sandoval and of Montoya, the disease has been considered to be of mycotic origin. Ruiz y Sandoval believed that there was only one species of fungus, and that the different colours of the patches were due to the different depths at which the fungus was growing. Montoya found a large number of different fungi belonging to the genera *Aspergillus* (*Aspergillus pictor*, etc.), *Penicillium* (*Penicillium montoyai*, etc.), *Monilia* (*Monilia montoyai*, etc.), and also fungi with intermediate characters between these genera.

During my stay at Porto Castilla and at Panama, I examined several cases for the presence of fungi, by microscopical and cultivation methods, and came to the conclusion that there are several varieties of pinta, the principal ones being yellow pinta black pinta and white pinta.

(1) *Yellow pinta.*—This term covers at least two conditions. In one, a fungus with all the characteristics of *Malassezia tropica* is found in great abundance; in the other, either no fungus of any kind, or at times microscopically a few yeast-like bodies are present. The first condition is in reality tinea flava. The non-mycotic patches are not raised and the borders are not usually so sharply defined. They represent a stage in a process of partial depigmentation, a stage in the progressive process of depigmentation from black to white, as in certain cases one can see all the stages from black, yellow, light yellow and white leukodermic-like. It must also be remembered that the fungi of tinea flava often produce a permanent or semi-permanent depigmentation. Syphilis, too, may cause depigmented patches.

(2) *Black pinta*, including the "bronzine" and the "blue" varieties. Under this heading too, several conditions should apparently be differentiated: (*a*) Patches of black or bronzine hyperpigmentation with occasionally a bluish tinge, not raised and not pruriginous, are seen; fungi are not found microscopically, or only as a few spore-like bodies on the surface of the epidermis; cultivation methods may show absence of fungi, or presence of penicillium-like, aspergillus-like, and other moulds identical with those which one finds at times on the skin of normal natives. The ætiological rôle of these moulds, so many species of which have been described by various observers, seems doubtful, and as regards the cases seen by me in Honduras, the organisms were in all probability only saprophytes. These patches of hyperpigmentation appear similar to or identical with the various chloasmas (bronzine chloasma, etc.), that are observed in natives and Europeans all over the tropics and are probably not of direct mycotic origin. (*b*) Patches of hyperpigmentation are seen, associated with or following infections with fungi of the group Trichophytoneæ (atrichophytons, epidermophytons, etc.). Some years ago I made the observation in Ceylon that chronic infections due to fungi of this group had in some cases a disturbing action on the pigmentation processes of the skin, which became either hyperpigmented, or less pigmented, or apigmented, and that these patches of hyperpigmentation and hypo-pigmentation remained visible for years after the fungus had disappeared. (*c*) Black patches, caused by the presence of *Cladosporium mansoni* (tinea nigra) in large numbers, are seen.

(3) *White pinta.*—Two conditions may be distinguished: (*a*) leukodermic patches, being the last stage in the process of depigmentation, which is represented first by amycotic yellow patches and apparently is not directly caused by the fungus; (*b*) depigmentation patches associated with or following chronic mycotic infections such as infections with the trichophytoneæ and tinea flava fungi.

Epidemiological notes.—The geographical distribution of pinta is very limited, the disease being found practically only in Colombia, Venezuela, certain parts of Central America and Mexico. A few cases have been reported from Brazil, and one or two doubtful ones from Africa.

The condition is certainly due to fungi, but according to several observers, e.g., Montoya, certain insects may play a rôle in the dissemination of the fungi.

According to Montoya, the fungi of pinta live saprophytically in certain waters, especially in those of mines, and of localities where the temperature is constantly high. Montoya obtained pure cultures of the pinta fungi direct from such waters. He has also found the same fungi as ectoparasites on the bodies of mosquitoes of the genus *Culex*, on sandflies (*Simulium*), and on the body of some bugs (*Clinocoris*), which are very common in the mines.

In some old chronic cases of pinta an acarus—somewhat resembling *Acarus scabiei*, though larger—has been found to live in the epidermal squamæ, and some writers believe that this acarus also plays a part in the transmission of the malady.

Predisposing causes.—What the older authors believed to be the true causes of pinta—viz., a hot, damp climate, insanitary surroundings and poor feeding, the mineral salts contained in the waters—are only predisposing causes, some of which,

however, are of great importance. The hot, damp climate favours the growth of the fungi; the water of the mines, which contains a large amount of mineral salts (especially sulphates), produces, after a time, in those who use it for washing, etc., a dermatitis, with fissures and other eczematous-like lesions which greatly facilitate the infection.

All races are liable to be attacked by the disease, but mulattos seem to be particularly prone to infection; albinos are said to be immune. Both sexes are equally liable, though males, on account of their occupation, are more frequently affected. The malady generally appears between the ages of 15 and 25, but it may appear at any age, and has been seen in children aged 3 or 4.

Cryptococcosis Epidermica.

This condition is characterized by dirty-looking patches, usually on the arms and legs. On scraping these patches, an enormous number of yeast-like bodies are found. The condition, so far, has only been found in the tropics. Both men and women are attacked; I have not seen it in children. It is probably transmitted by contact.

Trichomycosis Axillaris.

This condition is characterized by the presence of small nodules on the hairs of the axillary region. These nodules may be yellow, or red or black. The yellow nodules are caused by the fungus *Nocardia tenuis* Cast., the black variety is caused by a fungus, a black pigment-producing coccus, *Micrococcus castellanii*, Chalmers and O'Farrell.

The yellow variety has a cosmopolitan geographical distribution, being found in the tropics and subtropics, and in the temperate zone, including this country. It was very incompletely known for years as *leptothrix*. The red variety is common in the tropics and subtropics, rare in the temperate zone. The black variety seems to be purely tropical.

The disease affects both men and women, and is transmitted by direct or indirect contact.

Blastomycosis Cutis.

This disease is characterized by the presence of granulomatous framboesiform nodules, occasionally sinuses. It is caused by various fungi belonging to different genera. In the tissues, however, all these fungi appear in the shape of large, round or oval cells, with double contoured membrane and coarsely granular protoplasm. The principal species are the following: *Coccidioides immitis*, Rixford and Gilchrist, *Blastomycoides dermatitidis* Gilchrist and Rixford, *Blastomycoides tulanensis*, Castellani, *Blastomycoides lanuginosus* Castellani.

At one time it was believed that blastomycosis occurred only in America, but there is now no doubt that it occurs in many other countries, both in the tropics and subtropics, and occasionally in the temperate zone.

Men and women are equally attacked; it may be found in children and also in old people. The fungus apparently penetrates the skin through some small wound or abrasion. According to some authorities this fungus may live saprophytic in nature but we know nothing definite about it.

Acladiosis.

This mycosis is characterized by the presence of large circular or oval ulcers, sometimes covered by a thick rupioid yellow crust. It occurs in Ceylon, where I first described it, and also in the Federated Malay States, Southern China and Brazil. It is caused by a fungus of the genus Acladium (*Acladium castellanii*). We do not know anything definite about the transmission, but it is probably by contact, either direct or indirect.

TOKELAU (TINEA IMBRICATA.)

Clinical.—Tokelau, or tinea imbricata, is a mycosis of the skin, characterized by the presence of large, flaky tissue-like scales, up to ½ inch in length, firmly attached to the epidermis, partially covering each other like tiles on a roof—hence the name "tinea imbricata" given to the condition by Sir Patrick Manson. It has no tendency whatever to spontaneous cure. The pruritus is really terrible and the native patients refuse to do any work, remaining in their compounds, where they can be seen squatting or lying down and scratching their backs the whole day. Certain diets, for instance, a dry fish diet, makes the pruritus absolutely unbearable.

Epidemiological.—Tinea imbricata belongs to that small group of diseases which can be called "tropical" in a strict sense. No cases have been found outside the tropical zone. The home of tinea imbricata seems to have been originally the Malay Peninsula, whence it spread towards the south and the east to many islands of the South Pacific, northwards to some parts of China, as far as Foochow and Formosa, and westwards to Burmah. The Gilbert group of islands seems to have become heavily infected since the beginning of last century. In 1859, it is said that a native of Tamana, an island of the Gilbert group, affected with the malady, landed at an island called Tokelau in that year. From then onwards the disease spread rapidly all over the island. The Tamana man who brought the disease was called Peter, hence the disease became known in Tokelau as "Le Pita," i.e., "The Peter." From Tokelau the disease spread to Samoa, according to Turner and Köniğer, in 1869, and to many other islands, where it became known as Tokelau. At the present time it is extremely common in the Malay Peninsula, some parts of Indo-China and Southern China, Borneo, Samoa, Java, the Solomon Islands, New Guinea, Sumatra and Fiji. According to Daniels, the disease was first introduced into Fiji by some Solomon Islanders, in 1870, and within the following two years became extremely prevalent. In certain of the Pacific Islands, from one-third to one-half of the population is affected. The disease is common in some districts of the Philippine Islands, the Ladrones, the Loyalty Islands. New Caledonia, and some districts in Burmah. Until 1904 it was believed to be non-existent in Ceylon, but in that year I recorded the first case. During the last few years the disease has spread greatly in this island, and it is now fairly common, though not so common as in the Malay Peninsula or Fiji. India, so far, is said to be immune, but I have seen two typical cases hailing from Southern India. Cases have been reported from Brazil and other parts of Tropical America, but some doubt has been expressed as to their being cases of true tinea imbricata. The cases reported, so far, from Africa are also doubtful.

The climatic conditions favourable to the rapid development and spread of the disease are represented by a warm, damp, equable climate with a temperature of 80° to 90° F., the same climate, as Manson so truly remarks, that is favourable to the growth of cocoanuts; in fact, the geographical distribution of tinea imbricata corresponds almost exactly to the districts where cocoanuts thrive. In those countries which, although at certain times extremely hot, have a cold and cool season—such as many parts of India and China—the disease apparently does not spread.

Predisposing causes.—As regards age, many authorities state that the disease is more common in children than in adults. In Ceylon, however, the condition is rare or absent in infants and children and those affected are generally young adults, but it may be found also in old persons. Women are attacked less frequently than men. Villagers and people living in the country are much more liable to contract the malady than people living in large towns. It is doubtful whether there is any racial predisposition. In Fiji, however, it has been observed that, while extremely common in the indigenous population, it is comparatively rare among the immigrant Indian coolies. The Tongans also are said to contract the disease rarely, and this relative

immunity, according to them, is due to their habit of regularly anointing their bodies —a habit not shared by the Fijians.

Mycology.—Until a few years ago the disease was generally considered to be caused by fungi of the genus *Aspergillus*. While in Ceylon I was able to demonstrate that these fungi are really saprophytes; the actual causative fungi are organisms belonging to a totally different group, which can be grown at first only using special methods, which I called *Endodermophyton*. I succeeded in reproducing the disease in volunteers by inoculating cultures of the fungus which I had found, while the inoculation of the aspergillus-like fungi did not cause any lesion.

The infection is transmitted by contact, either direct or indirect.

Prophylaxis.—Some authorities recommend isolation; this is good wherever possible, but in regions where the disease is or has become endemic, usually the great number of people suffering from the affection render the measure impracticable. In those tropical countries, however, in which the disease has not yet appeared, the medical officers would do well to be on the look-out for it, and if a case is reported the patient should certainly be isolated and thoroughly treated before being allowed to mix with the general population, and all infected clothing should be boiled or burnt.

There is a general native belief that anointing the body with cocoanut oil, or other oil, will prevent infection; there may be some truth in this, but such a measure cannot be carried out in Europeans. I have seen an epidemic of tinea imbricata in a hospital in which a patient suffering from the disease had been admitted and allowed to mix with the other patients. Any itchy, scaly spot in the slightest way suspicious of incipient tinea imbricata, should be immediately treated with iodine, chrysarobin ointment, or resorcin dissolved in tincture of benzoin.

While the treatment of tinea imbricata in an advanced stage is extremely difficult, in fact almost hopeless, it is easy to check the initial patches by these means.

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Section of Medicine.

President—Dr. H. Morley Fletcher.

[*April* 26, 1932.]

Tuberculous Empyema.

By A. Brian Taylor, M.D.

Of recent years much attention has been paid to the problems of empyema and its treatment, but this has been concentrated mainly on types other than tuberculous. This special form differs widely from all others and requires different treatment.

Audouard [1], in 1838, was one of the first to appreciate that the principles of treatment of the ordinary type were not so sound with regard to the tuberculous empyema and that open operative treatment was inadvisable—but in effect it has only been the extension of the practice of artificial pneumothorax following the original work of Carson (in 1821) and Forlanini (in 1882)), and the consequent increase in incidence of the condition, that has directed closer attention to the problem. This paper is based on a review of the literature, and on experience gained at the Hospital for Consumption, Brompton. A search of the records at this Hospital during the past five years produced a series of 79 cases, which though from a statistical point of view not large, yet appears to be the longest single series of proved cases in the literature.

Pathologically, a purulent tuberculous effusion indicates pleural tuberculosis. A clear effusion may be a secondary exudate or an allergic response, but a purulent fluid must be the result of an actual tuberculous lesion in the pleura. This may be either primary or secondary. Fenton and Burrell [2] consider the former to be a definite entity—an inflammation of the pleura arising as a clear-cut disease without discoverable relationship to any pathological condition elsewhere, even if there is a latent co-existent disease of the lung.

The secondary variety is due to spread of the disease from the lung directly or via the blood-stream or lymphatics. The blood supply of the visceral pleura is through the lung, and the pleural lymphatics drain through the pulmonary vessels. Moreover, the common deposition of carbon particles in the visceral pleura from the lung shows how readily extension from the lung may reach the pleura.

The morbid process in the pleura follows the usual changes of a tuberculous lesion, beginning with œdema and slight exudate. The frequent occurrence of adhesions between the pleural layers at this stage explains the comparative rarity of tuberculous empyema, the focus of subsequent suppuration being confined within the granulation tissue of the adhesion. The rationale of treatment, by inducing pleural adhesion, is based on this natural process.

Subsequently, if adhesions do not wall off the lesions, a diffuse thickening and infiltration of the pleura may develop, or in other cases discrete tubercles form, and may be seen through the thoracoscope (Jacobaeus [3].) If the exudative process is then in advance of the proliferative process, effusion results, in the majority of cases clear at first, but sometimes purulent even from the beginning. Lilienthal [4] suggested that superficial caseation of scattered tubercles, or the

rupture of a large caseating focus into the pleura, determines the production of pus. Other factors influencing the nature of the effusion are the dose of the infection—tubercle bacilli are much more readily found in purulent than in serous effusions—and the resistance and immunity of the patient and of the pleura itself.

The ætiological conditions which occasion a purulent tuberculous pleurisy are numerous, but only a few main types are common. In my series of seventy-nine cases the following four groups are found:—

(1) Onset occurring in an artificial pneumothorax, 37 cases (46·8 %). One case followed the cauterization of adhesions.

(2) Onset by primary purulent pleurisy, 12 cases (15·2%).

(3) Onset in a previous serous pleurisy, 13 cases (16·4%). The average duration of the serous pleurisy before empyema was confirmed was 11½ months (the longest three years, the shortest one month).

(4) Onset after spontaneous pneumothorax, 18 cases (22·8%).

The following is a full list of causes from which a purulent tuberculous pleurisy may arise:—

(1) Insidious onset, no constitutional disturbance (cold abscess of the pleura), from: (i) Primary tuberculosis of the pleura; (ii) secondary pleurisy; (iii) miliary tuberculosis.

(2) From a serous pleural effusion becoming purulent: (i) A chronic effusion tends to become purulent in the course of time; (ii) repeated aspirations; (iii) increasing virulence of tubercle bacilli and greater chemotactic action (Floyd [5]); (iv) spontaneous absorption of the fluid part of the effusion (Fishberg [6]).

(3) With moderately severe onset, resembling that of serous effusion.

(4) With stormy onset; severe and extensive tuberculization of the pleura.

(5) Intermediate degrees between (3) and (4).

(6) Spontaneous pneumothorax. (i) Pure tuberculous infection: (*a*) pyopneumothorax; (*b*) pyothorax absorption of air (Fishberg's explanation of most cases); (ii) Primarily tuberculous with superadded secondary pyogenic infection: (*a*) Mild, little disturbance of health; (*b*) severe, "épanchements purulents, septiques et malignes" [7]. (iii) Pleuro-pulmonary fistula.

(7) Rupture of liquefied caseous glands into the pleural cavity, especially in children; this is rare (Scott Pinchin and Cartledge [8]).

(8) In association with artificial pneumothorax. (i) Extension of the pulmonary disease to the pleura: (*a*) Simple infection of the pleura with exudation; serous effusion becoming purulent; (*b*) rupture of caseous subpleural focus into pleural cavity; (*c*) spontaneous pneumothorax and pleuro-pulmonary fistula; (*d*) the same as (*c*) but with secondary pyogenic infection. (ii) Rupture of adhesions: (*a*) Tearing of lung at point of attachment; simple tuberculous infection of the pleura or spontaneous pneumothorax; (*b*) division in middle of adhesion and escape of infected material from drawn-out lung tissue; naturally or operatively (cauterization, etc.). (iii) Retrograde lymphatic metastasis. (iv) Hæmatogenous infection of the pleura. (v) Rupture of an effusion into a bronchus, with possibly secondary infection. (vi) During course of re-expansion of long collapsed lung—"transudate ex vacuo" (Alexander [9]). (vii) Late intolerance of the pleura (Dumarest [10]).

(9) In association with oleothorax.

The discovery of tubercle bacilli in the exudate is the best proof of the tuberculous nature of the empyema. In my series from the Brompton Hospital, tubercle bacilli were found in 66 cases out of 79; i.e., 83·5 %, but this is a much greater proportion than in most other reported series. Hedblom [11] found them in 4%, Netter [12] in 30%, Gloyne [13], in a short series, in 71%.

The diagnosis must frequently rest on the presence of a sterile effusion with a more or less chronic course and clinical features compatible with a tuberculous process. The clinical course may, however, vary widely, from an all but complete

absence of symptoms in the presence of a large purulent effusion, to a stormy onset with pain, fever, prostration and severe toxæmia.

The treatment of tuberculous empyemata presents problems of the gravest difficulty and the generally bad prognosis is discouraging. The lines along which effective treatment must proceed must be based upon: (1) The mechanical and toxic effect of the effusion itself; (2) the condition of the underlying lung, usually in some stage of tuberculosis; (3) the general health of the patient—the need and comparative value of radical or palliative treatment. It is useless to risk a patient's life to cure him of suppurative pleurisy when a pulmonary lesion is bilateral and advancing.

It is, however, when the trouble in the lung is slight or controlled, when a pneumothorax is otherwise producing satisfactory results, or when the patient's general condition is good, that treatment should be energetic and radical. It should be instituted early, even if the toxic signs are slight, as spontaneous recovery is rare and it is essential to husband the patient's strength.

The immediate necessity is the removal of the effusion; later an attempt must be made to prevent its re-collection. The former is best performed by gas replacement. This allows one to empty the pleural cavity almost completely, avoids marked changes of intra-pleural pressure, prevents sudden mediastinal displacements, allows X-ray control, keeps the pleura dry and permits a satisfactory adjustment of the intra-pleural pressure.

Occasionally one or more gas replacements, by drying the pleura and removing the toxic fluid, result in healing of the pleura and cure of the condition. More often, further treatment is needed. Pleural lavage is often helpful. After gas replacement, with two needles still in place, antiseptic lotion is run into the pleural cavity which is then aspirated, the intra-pleural pressure being controlled throughout. Dakin's solution and most of the aniline dyes have been recommended among others for this purpose. The first has the advantage of dissolving lymph clots and tending to soften a thickened and rigid pleura so as to promote healing. Hippocrates was the first to recommend this procedure and now Burrell [14] and R. A. Young, in his Lumleian Lectures [15] have endorsed it. Among the advantages of the method is the beneficial effect on the diseased pleura itself of lavage with antiseptic and saline solution; disinfection of the pleural cavity is hastened, tubercle bacilli disappear sooner and the fluid becomes thinner and more serous. In secondarily infected cases it will sometimes sterilize the effusion and obviate more drastic surgical treatment.

By continuing pleural lavage, combined with gas replacement to keep the pleural cavity dry and empty, the lung may be gradually re-expanded to such an extent that by adhesion between the two pleural layers radical cure is produced. After each operation, a negative pressure of from 10 to 20 cm. of water is left, and by maintaining this over a number of weeks the lung is drawn out. When the lung is brought constantly into contact with the parietal pleura, adhesion will occur and further effusion is prevented. Finally, the whole cavity may be thus obliterated. Certain conditions must, of course, be present before this successful result can be achieved. It is evidently useless to re-expand a lung containing active tuberculous disease, or where re-activation of old disease is likely to occur. After artificial pneumothorax has been maintained for over two years for a lesion originally slight, it is fairly safe to expect the lung to be healed. Or with a purely pleural lesion and the knowledge of a more or less normal lung beneath, its re-expansion is not contra-indicated. In suitable cases treated successfully in this way the results are brilliant.

Another useful method in treatment is that of pleurotomy with constant drainage. When secondary infection has occurred and pleural lavage does not control the effusion and toxæmia, or when re-collection of the effusion is so rapid that reasonably spaced gas replacements are insufficient, or when a pleuro-pulmonary fistula is present

and persists, some form of constant drainage is required. A de Pezzar catheter placed intercostally is often sufficient, and by drainage under water at a low level a steady negative pressure is developed which gently pulls on the lung and keeps the effusion drained and away from any fistula, which is thus given a chance to heal.

Rarely does this procedure produce permanent cure. A sinus persists indefinitely, the chest wall may become infected and the effusion, if not already so, becomes secondarily infected. The method is therefore useful only as a temporary measure, or when the patient is too ill for radical treatment, and gives relief only for a short time.

Oleothorax, in the treatment of tuberculous empyema, originated from the work of Bernou [16], and Kuss [17] in France, where it has had a considerable vogue. In this country a few writers have reported success in the use of the method, but experience at the Brompton Hospital has not been very encouraging. Gilbert's [18] review of the subject in 1930 gives the following as the advantages of the method:—

(1) Disinfection: with the olive oil introduced, a 5 % to 10 % addition of gomenol is commonly made, for its antiseptic properties.

(2) Indirect detoxicating action, by making the pleural layers thick and impermeable.

(3) The mechanical action of replacing the effusion with oil may hinder the re-collection of pus.

The method is mainly indicated in recurring purulent pleurisies when it is desired to maintain collapse of the lung, in cases in which the toxæmia is severe, in cases secondarily infected before surgical treatment is begun, or in the presence of pleuro-pulmonary perforations which may be healed by the oil. On paper, the evidence in favour of the use of oleothorax is strong, and a number of writers are enthusiastic, but my own experience of it in practice has led me to use it only in exceptional cases.

Finally, the use of thoracoplasty has provided one of the most valuable methods, and is making the outlook in individual cases much more favourable. This operation attempts to achieve radical cure in a similar way to that of repeated gas replacements and pleural lavage, by bringing the pleural layers into firm contact and inducing uniform adhesion, but in this case the chest wall is brought down to the lung instead of the lung being expanded out to the chest.

When there is active disease in the lung on the affected side only, or when the disease has been locked up by fibrosis and scarring, and re-expansion would be dangerous, thoracoplasty is the operation of choice. The case must, of course, be carefully chosen under the same rules as those which govern the choice in other conditions. The condition of the contralateral lung, the general resistance and vitality of the patient to withstand the operation, and the absence of complications must be considered before operation is advised.

Phrenic avulsion is preferably performed first; it reduces the size of the cavity to be obliterated, it tests the other lung under conditions of increased mobility, and it puts at rest the actively diseased lung and pleura. Subsequently a paravertebral thoracoplasty is performed, usually in two stages. An extensive resection is needed in most cases, such as the subscapular operation of Brauer. Resulting from the operation, the remaining portions of ribs fall in and compress the parietal towards the visceral pleura. The pleural cavity may need frequent emptying as the collapse takes place, aided by a special belt and the use of heavy weights laid on the chest wall. In successful cases, the pleural cavity is more or less completely obliterated and the suppurative pleurisy checked. At the same time the diseased lung is kept compressed and immobile to allow of healing of the pulmonary lesions.

The result of treatment in any series of cases is never encouraging, as so many of the patients are in late stages of advanced disease and nothing will avail to save them. Moreover, in other cases, though the empyema is cured, the pulmonary lesion is not affected and progresses in spite of sanatorium or other treatment.

Of the 79 cases occurring at the Brompton Hospital between 1925 and 1930, the results of treatment reviewed in 1931 were as follows :—

NUMBER OF CASES 79: MALE 54 (68·4%); FEMALE 25 (31·6%). AVERAGE AGE 30·5 YEARS.

Years	Cases	Percentage
Between 0 and 20 ...	14 ...	18
,, 21 ,, 30 ...	33 ...	42
,, 31 ,, 40 ...	22 ...	28
,, 41 ,, 50 ...	6 ...	7
,, 51 ,, 60 ...	4 ...	5

Results: 25 alive in September, 1931 (31·6%); 46 dead (58·2 %); 8 not traced (10·2%).
Average time of survival from onset of empyema: Dead 1·6 years; alive 3·7 years.
Average time of survival from onset of pulmonary tuberculosis: Dead 3·6 years; alive 6·9 years.
Tubercle bacilli found in pus from the empyema in 66 cases (83·5%).

Pleural wash-outs alone were used in 18 cases, with a 50 % mortality, and in addition to gas replacements in 57 cases, with a mortality of 52·6 %. Eleven cases treated by drainage alone had a mortality of 63·6 %, but these were mainly the severe and advanced cases. Thoracoplasty was employed in 13 patients and 4 were dead in 1931—i.e., a mortality of 30·8 %.

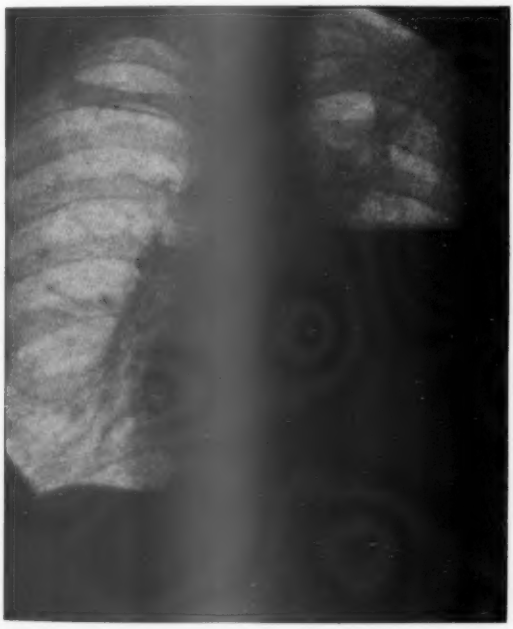
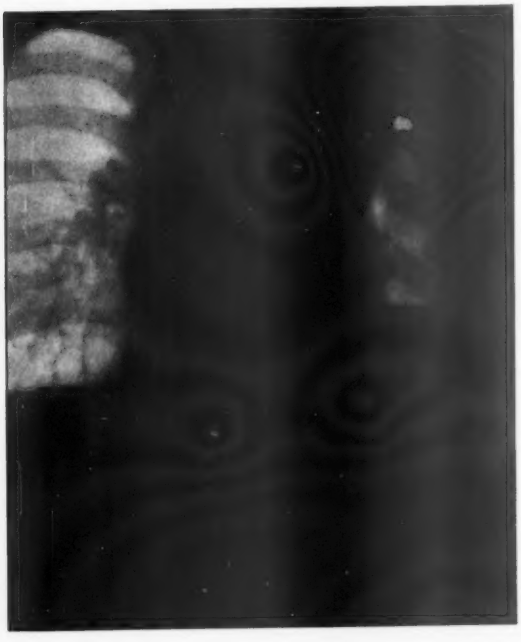


FIG. 1.—*Case I.*

26.6.29. Pulmonary tuberculosis began in 1923; left pleurisy in 1926; purulent effusion found in 1929. Gas replacement reveals much disease in underlying lung. R. lung good. Recommended for thoracoplasty.



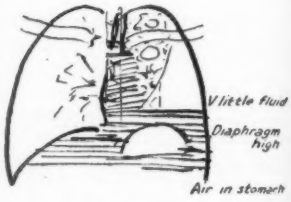


FIG. 2.—*Case I.*

23.7.29.—After left phrenic avulsion. Left side of diaphragm high and showing paradoxical movement. Right lung — no change with increased work, i.e., no active lesion to contra-indicate thoracoplasty.

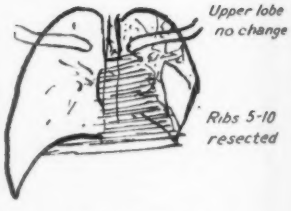
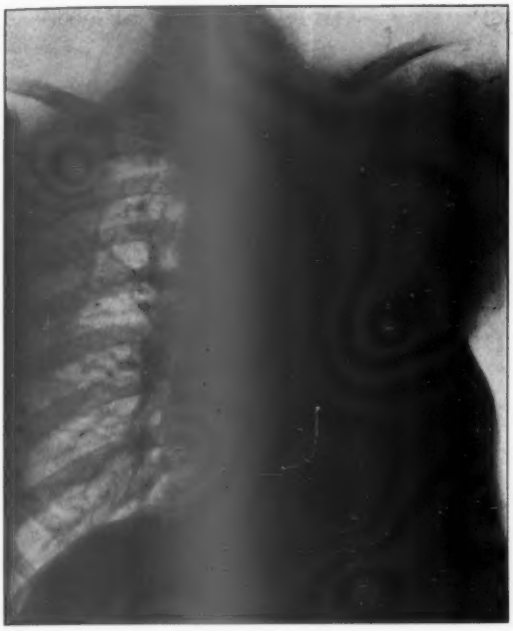


FIG. 3.—*Case I.*

13.8.29. After thoracoplasty, first stage. Resection of ribs 5 to 10. The base has collapsed well.



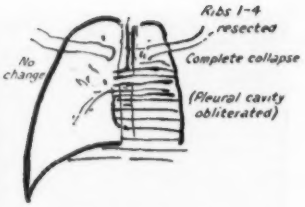


FIG. 4.—*Case I.*

12.2.31. Thoracoplasty, second stage, 14.8.29. Condition six months later: satisfactory collapse of chest wall obliterating pyopneumothorax cavity. Right lung good, mediastinum, etc., not displaced. Previously febrile and emaciated; now no symptoms and putting on weight.

FIG. 5.—*Case II.*

24.9.30. Left artificial pneumothorax induced in 1928 for unilateral pulmonary tuberculosis. Good progress until a chill; then effusion into pneumothorax cavity becoming purulent, with symptoms of toxæmia. Gas replacements and pleural wash-outs instituted to induce lung to re-expand and adhere to parietal pleura, so obliterating the pyogenic cavity.

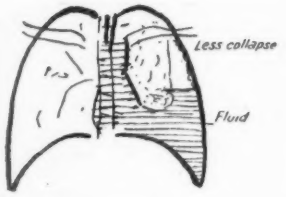


FIG. 6.—*Case II.*

13.10.30. Considerable re-expansion of lung after frequent pleural wash-outs, but later stages prolonged owing to much thickened pleura. Toxic absorption obviated and general condition remains excellent. Contralateral lung unaffected.

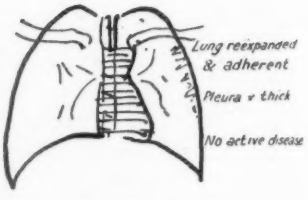


FIG. 7.—*Case II.*

27.1.31. Complete expansion of left lung; pleural cavity obliterated by adhesion of much thickened visceral and parietal pleuræ. Some fibrosis and bronchial catarrh in both lungs only. Patient cured and back at work.

In conclusion, it is evident that tuberculous empyema is a severe disease, usually complicating pulmonary tuberculosis. If the latter underlying disease does not seriously affect the prognosis in itself, treatment of the empyema by repeated gas replacements and pleural lavage, and later an attempt at radical cure by producing adhesion between the pleural layers, either by re-expanding the lung or by collapsing the chest wall by thoracoplasty, is a rational procedure likely to give benefit to the patient. The empyema may be completely cured or at least considerably improved.

I have to thank the staff of the Hospital for Consumption, Brompton, for the use of case notes and skiagrams and for valuable advice.

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Section of Obstetrics and Gynæcology.

President—Mr. VICTOR BONNEY, M.S.

[*June* 17, 1932.]

Modern Methods of Alleviating the Pains of Child-birth.

By L. C. RIVETT, F.R.C.S.

ANÆSTHETICS were discovered about a hundred years ago. The first was nitrous oxide; ether and chloroform followed, and it was just over eighty years ago that Sir James Simpson used this latter drug to alleviate the pains of child-birth. He met with considerable opposition until he persuaded Queen Victoria to have chloroform for the birth of her seventh child in 1853. About thirty years ago, Kronig and Gauss, of Freiberg, introduced "twilight sleep." More recently the addition of oxygen and nitrous oxide has enabled us to administer the gas for a prolonged period. More recently still, the introduction of the barbitone series (nembutal, pernocton, &c.), which can be taken per mouth or injected intravenously, has provided us with powerful anæsthetics which are, as yet, in the experimental stage. Spinal anæsthesia has been employed, and rectal ether and avertin can be used in suitable cases.

In this paper I hope to show that it is now possible to alleviate the pains of labour in over 90% of normal deliveries. It is solely with normal deliveries that I am concerned, and I want to make it quite clear at the outset that I am not considering anæsthetics for obstetric operations.

About three years ago an opportunity to extend this proposition was presented to me. Lady Rhys Williams—and later, Mrs. Baldwin—raised a fund to provide facilities for administering some form of anæsthetic to patients in lying-in hospitals. Queen Charlotte's Hospital accepted their offer and appointed first one, and later two, resident anæsthetists, whose main duty was to deal with cases of normal delivery. Even before this time the Middlesex Hospital had instituted a similar service in its lying-in wards. Experimental work has been carried out at both these institutions with a view to discovering an ideal method which is applicable to practically all cases of normal labour.

During the course of my professional life, I have had practical experience of most methods of relieving the pain of child-birth, and I now propose to consider them seriatim.

I think the first to claim attention is the oldest anæsthetic—nitrous oxide gas. This gas was discovered by Sir Humphry Davy in the year 1800, and some thirty years later was used in dentistry. The early impure gas was only suitable for producing anæsthesia of very short duration, and obviously had no place in labour. In recent years the addition of oxygen to the purified gas has given us an anæsthetic which can be used for indefinite periods, and with a modern re-breathing apparatus it is about as safe as anything can be in this uncertain world. It is true that fatalities have occurred during the administration of these two gases, but they are so rare that they do not require much consideration. As an analgesic it is practically ideal. It produces complete unconsciousness and therefore absolute relief from pain. It can be administered for as long as normal labour is likely to last, and it can be reinforced by the addition of a little ether, if more relaxation is required for the actual delivery of the head. It can be discontinued and the patient comes out of its effects in one minute or so. Finally, it does not appear to inhibit uterine contractions, so that the course of labour is not delayed by its use. This has been shown by Bourne, who introduced a bag between the membranes and the uterine wall, and connected it to a tambour with a recording pointer working on a drum. Both ether and chloroform markedly reduced the uterine contractions as recorded on the drum, but nitrous oxide and oxygen had practically no effect.

Now as regards the drawbacks. Gas-and-oxygen can only be administered by means of a tightly fitting mask. After prolonged use this causes discomfort, especially if the gas is administered intermittently, as is required in the first stage of labour. The apparatus for its administration is large and heavy, and obviously is not ideal for administration in domiciliary obstetrics. It requires a very high degree of skill for its successful administration for several hours on end, and really can only be used by someone who has had special training and a considerable amount of experience. Lastly, it is expensive. More than half the confinements which take place in England and Wales are conducted by midwives alone, and general economic conditions do not permit of the universal use of this form of anæsthesia for 600,000 confinements per annum. For the wealthy, who can afford to pay a skilled anæsthetist £3 3s. an hour for ten or twelve hours or more, it would be difficult to surpass.

Twilight sleep, the popular name for morphia-scopolamine narcosis, is another ideal analgesia. I do not need to go into the details of the administration of this drug. Its few drawbacks can be shortly summed up as follows: It occasionally causes a complete cessation of uterine contractions: these invariably come on again later, and the only drawback is delay. It is possible that this effect is due to the drug being administered too early in labour; anyway, it is not a serious defect. It tends to prolong labour, and in my experience more cases require assistance by the forceps to complete delivery. The baby is sometimes born in a state of apnœa, and may be difficult to rouse, but I have not had any infant deaths that I have been able to ascribe to this cause. On rare occasions the hyoscine acts as an excitant, and the patient becomes maniacal. This condition is alarming and troublesome at the time, but it soon passes off and the patient has no recollection of it, or of the labour. The noise, however, is a distinct drawback in domiciliary practice, as the relatives all think the worst is happening. Also the number of attendants in a private house is usually insufficient to control the patient. To obtain really successful results it is essential that a skilled and experienced attendant should be constantly present throughout the labour, so that the dose may be varied according to the state of amnesia. In a modified form it is very useful in dulling the pain, and perhaps more particularly the memory of the pain.

Spinal and sacral anæsthesia are of too short duration to be of real value in normal labour. Spinal anæsthesia appears to inhibit the action of the longitudinal muscle-fibres of the uterus, and at the same time to increase the contractions of the circular fibres. The result is a violently contracting uterus with very poor expulsive powers.

Rectal ether-and-avertin has been used. At Queen Charlotte's Hospital we found difficulty in keeping it in the rectum. Perhaps we did not inject it properly or at the proper stage of labour. At any rate we found that it was apt to be expelled during the next few pains. I have recently read a paper by O'Donel Browne, of Dublin, describing a combination of morphia, intramuscular injection of magnesium sulphate and rectal ether and quinine; the results are so good that I intend to try the method.

Oral or intravenous administration of nembutal or pernocton appears to offer possibilities of being quite ideal. At present these drugs are still to a certain extent in the experimental stage. We have tried them in a few cases, and have obtained varying results, some very good, others not so. I intend to carry out further research in these drugs, and I think that if we could devise a formula to calculate the dose for each individual, we should be able to ensure that the patient felt nothing for twenty-four hours.

Ether is not at all suitable for normal labour. If administered in very small doses it is likely to produce more of an excitement stage than a narcosis. If administered over a long period, it tends to irritate the lungs and cause bronchitis or even pneumonia.

Over eighty years ago, Sir James Simpson advocated the use of chloroform to abolish the pain of labour. This was the first anæsthetic to be used in labour, and I think it is still the best. It is not the ideal analgesic, and I do not for a moment advocate the administration of pure chloroform to produce surgical anæsthesia for obstetric operations. It is dangerous for this purpose, as it is so easy to give an overdose with either immediate disaster or remote delayed chloroform poisoning. But with the small amount necessary to abolish all pain of labour there is no risk whatever.

I do not think it is generally realized what a small amount of chloroform is required to abolish completely all sensation of pain in labour. "A few whiffs," is usually interpreted to mean very light anæsthesia. But anæsthesia is not necessary at all. In fact it is detrimental to the progress of labour. Little more than the smell of chloroform produces a state of analgesia in which the patient does not feel any pain, yet is conscious of every uterine contraction, and is able to bear down to assist the expulsion of the child.

Chloroform can be administered either by means of a drop-bottle or through a Junker's apparatus. It can be given during the first stage, as soon as the pains begin to hurt, and provided that the patient is not rendered unconscious, it can be kept up for twelve hours without any untoward effect whatsoever. The important factor is that only the smallest amount should be given, and that only when the patient, who should be perfectly conscious, states that she feels a pain coming. In the intervals the mask is removed from the face altogether. Towards the end of the second stage it should be given continuously, especially if the administrator is also the accoucheur, as sufficient would then be inhaled to abolish the pain of the actual delivery through the vulva.

When chloroform is given in this way it does not retard labour. It is true that the contractions recorded on the drum by Bourne showed diminution in height and decreased frequency, especially the latter, but labour progresses in spite of this, and I think that this is due to the lessened resistance of the soft parts, owing to the abolition of the pain reflex which normally causes spasm of the cervix and levator ani muscles. In actual fact, labour, particularly the second stage, seems to be shortened, and at the Queen Charlotte's Hospital, where the routine has been to begin chloroform analgesia directly the second stage commences—as indicated either by the pains becoming bearing-down in character, or by the membranes rupturing—it has been found that the average duration of the second stage is forty-five minutes in primigravida and under half an hour in parous women. The incidence of forceps was not increased, nor were perineal lacerations more frequent. At Queen Charlotte's Hospital, over two thousand cases have had chloroform analgesia, and in no single case has there been any untoward result, although in a very small percentage it has not been successful, in that the pain has not been abolished, and in very rare cases a state of excitement has been produced, due, I think, to the analgesia having been begun too late.

At the Middlesex Hospital chloroform analgesia has been practised for the last six years with almost exactly similar results. Here the indication has been to step in with the chloroform as soon as the pains are of sufficient violence to cause the patient to cry out. "Silence in the labour ward" has been our motto.

Not only was the Middlesex the first Hospital to employ routine administration of chloroform as an analgesic, but it was the pioneer hospital, about six years ago, in sanctioning the administration of chloroform by midwives to all the patients who had been passed in the antenatal department as being normal obstetrically, and having sound heart and lungs—and this without further reference to the resident medical officer in charge of the department.

For five years Junker's apparatus was used. The experiment has been an absolute success and, as in the case of Queen Charlotte's Hospital, there have been

no untoward results, no increase in the incidence of forceps application, and no more frequency of perineal lacerations.

To return to the economic side of the question. If at least 90% of 600,000 women per annum are to have the pains of labour abolished, it is obvious that the analgesic must be in the hands of midwives. Even when a doctor is engaged to conduct a normal confinement, it is not possible, under the present arrangements of medical services, for him to spend from ten to twelve hours in attendance on one case. At all events, doctors attend less than 50% of the confinements in England and Wales. In most cases a midwife conducts the case alone, and even if not, a midwife is in attendance, either living in the house, or there for the duration of labour, and for the greater part of the time she has nothing much to do.

I am endeavouring to evolve a safe method of producing analgesia which can easily be taught to midwives. Administration of chloroform with a Junker's apparatus is extremely convenient, easy and satisfactory, but from the point of view of its being extensively used by midwives there are two possible objections: (i) The tube can be connected up the wrong way, or the bottle tilted, so that liquid chloroform is sprayed on to the patient's face. (This difficulty is quite overcome in the new modification of Junker's apparatus.) (ii) It is possible, by vigorous work with the bellows, to produce quite deep anæsthesia. This is the only serious objection. In the hands of any intelligent midwife it is negligible, but if we are legislating for the masses, it may mean a real danger.

I have had a small amount of chloroform put up in glass capsules, similar to those in which amyl nitrate is put up, which can be crushed with the fingers, and so liberate the chloroform. Each capsule contains 20 minims of chloroform, and is wrapped up in gauze. In use a capsule is crushed and tucked in under the edge of the frame of a Schimmelbush mask, and the mask held over the patient's face coincidently with each pain. From six to ten capsules an hour produce complete analgesia. Now I submit that by this method it is quite impossible to give an overdose. And further, the method is so simple that any midwife could have in it a course of instruction within a month or two, and would then be capable of administering the drug with perfect safety.

The sister-midwives at Middlesex Hospital have been using the capsules for nearly a year, and at Queen Charlotte's Annexe one sister-midwife has been using them for three months, also without direct medical supervision.

I have a complete report of 200 cases at the Middlesex Hospital. The results are as follows:—

TWO-HUNDRED CASES OF CHLOROFORM CAPSULE ANÆSTHESIA.

	No.	Percentage
Good	146	73
Fair (1 breech)	42	21
Poor	4	2
Perineal lacerations ...	6	3
Hysterical	1	0·5
Post-partum hæmorrhage ...	1	0·5
Deaths	0	0

All four cases recorded as poor did not have sufficient; two had two capsules per hour, and the others, four capsules per hour. The hysterical case was the sixth of the series, and in spite of the hysteria the result was "fairly good." I do not think the chloroform had anything to do with the post-partum hæmorrhage, and in any case 0·5 % is not a very high incidence.

I am much indebted to Miss F. M. Parsons, late Resident Anæsthetist at Queen Charlotte's Hospital, for her co-operation in the early stages, and also for a laborious piece of work that she carried out for me. I wished to know how many deaths in England and Wales were due to anæsthetics in childbirth. By the courtesy of the Assistant-Registrar at Somerset House, we had access to an unpublished file of anæsthetic deaths, and Miss Parsons undertook to extract from these. The

records are so incomplete that I cannot determine whether death was in any way due to the anæsthetic, or was due solely to the accompanying "operation."

In a table which we compiled recording all the deaths associated with anæsthesia during ten years, it was interesting to note the steady increase in the total, and how exactly the percentage of cases during child-birth had kept level with the total deaths. Out of 314 cases, the details of which Miss Parsons extracted, in only two could death possibly be ascribed to the anæsthetic, and even in these doubtfully so.

I hope I have made out a case that in the ampoule method of administering chloroform we have a means of alleviating the pain of labour in at least 90% of normal deliveries, which may safely be entrusted to midwives, after due instruction in the details of the method. I hope that a resolution will be passed requesting the Central Midwives' Board to inquire into the possibility of issuing certificates to midwives who have received the necessary instruction and satisfied the authorities, stating that they are proficient to administer light anæsthesia for normal deliveries.

Conclusions.—Nitrous oxide and oxygen is the best anæsthetic, but has the disadvantages of requiring a cumbersome apparatus, and a specialist to administer it, and of being expensive. Chloroform in minute doses is safe, cheap, and satisfactory, and can be administered by midwives. The capsule method is easily and quickly learnt. The barbitones, avertin and rectal ether ought to be further investigated. With correctly calculated dosage they may be very valuable in domiciliary obstetrics.

Discussion.—Mr. R. H. PARAMORE (Rugby) said the suggestion that capsules of chloroform should be given by midwives was a good one, but he advocated spinal anæsthesia and episiotomy, together with forceps delivery.

Dr. J. S. FAIRBAIRN said that he would confine his remarks to the need for analgesics suitable for administration by midwives. The midwife-employing class must be maintained at as high a proportion of the community as possible, because it succeeded in producing the maximum percentage of natural deliveries, and therefore had the lowest maternal mortality. But such aid in the relief of pain as could be given to their better-off sisters must be made available also for them. The medical practitioner was too expensive a social instrument to employ in attendance on normal labour, and, the time taken up in maintaining these lighter forms of anæsthesia or analgesia that did not interfere with the course of labour must be lengthy, so that they were out of the question for the busy general practitioner.

The Central Midwives' Board could not undertake the responsibility of laying down training and certifying midwives for such a purpose, as suggested by Mr. Rivett. It was a statutory body with its powers defined and limited by Act of Parliament, and such an addition, even if desirable, was impossible without legislation. The Board was free from blame in preventing the use of many of the sedative drugs mentioned, for one of the subjects of instruction and examination of pupil-midwives was the administration of such drugs as might be required in midwifery. But owing to the prejudices of lecturers and local health authorities, and the fear that any drug mentioned in the Dangerous Drugs Act was therefore too dangerous for use by midwives, this instruction had never been properly carried out and many local authorities had exceeded their function by making local rules of their own to prohibit midwives from using any analgesics. Hence it was important that this method of giving 20 drops of chloroform in capsules should be fully tried-out under medical supervision, so that its value and possible risks might be thoroughly investigated.

Mr. HERBERT CHARLES said that with regard to the barbiturates the results had not been very convincing, as one could not be sure of getting exactly the same results in each case. Ether was very objectionable; patients were often sick during a prolonged—though light—ether anæsthesia. He did not know why so many people were afraid of chloroform: he had been "brought up on it," so to speak, and although admittedly he always treated it with the greatest respect, it gave him much the best results in the early stages of labour. The early anæsthetic stages with chloroform were much longer than with any other anæsthetic, therefore one had greater ease in keeping the patient in the analgesic stage. With chloroform the pains were almost instantly abolished, although the patient was wide awake and could express her gratitude for the relief; the uterine contractions in this early stage did not seem to be affected. A Junker's bottle was a very useful apparatus, but the method suggested by Mr. Rivett of giving capsules of 20 minims of chloroform on a

mask was certainly the most convenient one, and if these capsules were used only occasionally there was no fear of overdose.

Dr. A. J. COPELAND said that chloroform capsules, used in a short series of cases at Queen Charlotte's Hospital, had, in his experiments, been ineffectual. They were used at the end of the second stage. He suggested that the following precautions should be printed on the paper enclosing each capsule : (1) Use only one capsule every five minutes; (2) hold the capsule in a mask or in lint (not handkerchief) two inches from the patient's face; (3) keep the face uncovered.

Nembutal given by mouth, with choral, every two or three hours, gave varying results. The routine adopted was that of O'Sullivan and Crane [1] in 23 cases. Analgesia and amnesia were perfect in some cases, especially in one—that of a primapara aged 14½ years, who received 3 grains of nembutal and 20 grains of chloral in the middle of the first stage, and was delivered three hours later. She remained in a state of hypnosis, and no further anæsthetic was required, but some oxygen was given after delivery to counteract slight cyanosis and apnœa. She retained no recollection of the labour. In a few cases the patients became excited, and in one case there was imperfect relaxation of the uterus, which necessitated chloroform. Minor disadvantages were slight cyanosis—relieved by oxygen—and headache. Further research appeared to be advisable, and, to secure better results, it should be carried out in quiet rooms—not in labour wards—as the patients were roused by noise. During anæsthesia and analgesia in labour, oxygen was of great value in helping to maintain uterine contractions. For hospital work, Boyle's apparatus gave ideal results; with this apparatus the analgesia and regular uterine contractions could be maintained for as long as necessary. For the sake of economy, large cylinders (750 gall. nitrous oxide, 240 gall. oxygen) should be used in hospitals. A good method suitable for private work was to give chloroform, on lint or a mask, up to a stage of light anæsthesia, when the head was showing, and then to give oxygen from a small cylinder every few minutes, to maintain the uterine contractions.

Miss D. C. LOGAN spoke on the value of anæsthesia obtained by Junker's apparatus.

Dr. R. A. GIBBONS said that the chloroform capsules would be a great convenience for administration by the nurse until the arrival of the doctor or anæsthetist; they were perfectly safe, as the nurse would know from the doctor's instructions at what intervals they were to be administered. He presumed it was not suggested that they should be used after the arrival of the doctor or the anæsthetist. He had always used chloroform, and had trusted competent obstetric nurses to administer, when necessary, a few whiffs as each pain came on before his arrival. He never used an anæsthetic during the first stage. The chloroform was given in an open mask, a little as each pain occurred, the patient being conscious between the pains, until the head was passing, when the anæsthesia could be as deep as required. Sometimes towards the end of labour, when the patient seemed exhausted, he had asked the anæsthetist to use ether. Gas with oxygen was ideal, but so inconvenient, owing to arrangements having to be made beforehand, that it was practically impossible if one had many cases to attend. The anæsthetist had to give his undivided attention to the anæsthetic and the apparatus, and was not available to give any assistance for a few seconds in getting the patient into proper position if forceps had to be used, as was the case when the administration was with an open mask.

Mr. RIVETT, in reply, said that when chloral and potassium bromide were given during the first stage the patient felt a good deal of pain, although she became drowsy and rested between pains.

He agreed with Dr. Boyle that gas-and-oxygen was delightful, especially when administered by Dr. Boyle, but it required considerable skill to administer it continually for many hours. He did not agree that ether was suitable for normal labour. If it was administered in small quantities it produced excitement, and if given in greater concentration for a prolonged period, it produced pulmonary complications.

The idea of the capsules had been suggested to him by Miss Edith Pye, President of the Midwives' Institute. He had given chloroform by this method for hours on end to private as well as to hospital patients. They talked all the time and did not lose consciousness, but felt no pain and were well and comfortable afterwards. If really small amounts were used the contractility of the uterus was not affected.

Chloroform was not included under the Dangerous Drugs Act, so that a midwife could now purchase it without any restriction. Hyoscine was scheduled as a dangerous drug.

1 *Lancet*, 1932, i, 119.

Section of Therapeutics and Pharmacology.

President—Dr. E. P. POULTON, F.R.C.P.

[*May* 24, 1932.]

DISCUSSION ON SOME PROBLEMS CONCERNING THE PREVENTION AND TREATMENT OF ACUTE RHEUMATIC INFECTION.

Dr. W. R. F. Collis: The French school have for many years held acute rheumatism to be an infectious disease. Grenet described five epidemics of rheumatic fever during the late war. He showed how the disease remained in a certain unit although that unit was removed from its position in the line—cases occurring in its new quarters, while the relieving troops remained free from the disease. He considered this to be evidence in support of the view that infection is a more important factor than environment in the causation of acute rheumatism. Seventeeen years ago he made the following prophecy: "Je me crois donc autorisé à déclarer que le rhumatisme articulaire aigu est une maladie contagieuse, conception qui me paraît présenter une grande importance doctrinale et qui peut-être aura un jour une réelle importance pratique." Dr. Bradley and I hope to show to-day that this prophecy has now been fulfilled, and that the conception of rheumatic fever as a contagious disease is now of practical importance.

Glover in 1930 described epidemics of tonsillitis occurring in semi-isolated communities at Army and Air Force establishments. He showed that the peaks of these tonsillitis epidemics were followed after a period of two weeks by the peaks of rheumatic fever, and was able to show a correlation between over-crowding, tonsillitis and rheumatic fever.

Swift in 1930 strongly emphasized the importance of tonsillitis preceding rheumatic fever. He recognized the fact that acute tonsillitis is usually associated with hæmolytic streptococcal infection, and hence commenced, some years ago, a new line of therapy, using small doses of hæmolytic streptococci in the form of an intravenous vaccine for rheumatic subjects, the rationale of this method being to attempt to desensitize the patient to the products of the organism.

Schlesinger, while in charge of a convalescent home for rheumatic children at West Wickham, observed the after-effects of epidemics of sore throat among the rheumatic patients, and he found a constant sequence of events. The patients first suffered from an acute nasopharyngeal infection lasting from two to five days. They seemed to recover completely from the throat infection, the temperature and pulse returning to normal. Then followed a "silent" period of from ten to twenty days, during which the children appeared perfectly well. At the end of this period a rheumatic relapse, either arthritic or carditic, suddenly developed. The organisms associated with the epidemics of throat infection at West Wickham were not isolated.

During the winter 1930-31 a group of twenty-five convalescent rheumatic children in Dr. Wilfrid Sheldon's ward at the Cheyne Hospital, Chelsea, were kept under observation by him (Dr. Sheldon) and myself. The throat flora of the

whole ward was examined at regular intervals and hence any throat infection which occurred was immediately detected.

On November 1, 1930, a serious epidemic of nasopharyngeal infection commenced, spreading from case to case. In all, thirteen children were infected, and of these eight subsequently developed an acute rheumatic relapse.

The "silent" or "incubation" period mentioned above was well shown in this epidemic, and varied from seven to twenty-four days. The following case is a typical example:—

Case 1.—Girl, aged 7, convalescent rheumatic patient in Dr. Sheldon's ward at the Cheyne Hospital. The condition of the child appeared satisfactory in every way, the heart was well compensated and there was no evidence of active rheumatic disease. On November 11, 1930, an acute tonsillitis developed, accompanied by a rise of temperature to 102° F. The throat culture revealed the presence of a pure growth of hæmolytic streptococci. In three days all the symptoms had disappeared, and the child appeared to have recovered. No symptoms appeared until November 25, 1930, when the temperature and pulse suddenly rose, and acute rheumatic pericarditis, with extreme cardiac dilatation, set in.

The organism isolated in this epidemic was the hæmolytic streptococcus, but it was only during the height of the throat infection that the organism could be obtained in anything like pure culture from the pharynx. It tended to disappear rapidly, as shown by successive throat cultures, and often could no longer be found towards the end of the silent period. This observation explains why the reports of previous writers on throat infection in acute rheumatism have often been negative. Being unaware of this "silent" or "incubation" period, they made throat cultures only after the appearance of the rheumatic symptoms, and thus failed to find the causal organisms of the initial throat infection in preponderating growth.

Numerous blood-cultures were taken during the initial tonsillitis, in the "silent" period and during the subsequent acute rheumatic relapse, but the hæmolytic streptococcus was never grown. It is interesting to note, however, that cultures taken at autopsy in four fatal cases revealed the presence of the organism in locations as far distant from the throat as the spleen and the pericardial glands. These results have been confirmed subsequently on a much larger series of cases.

Skin tests with an extract of the hæmolytic streptococcus, termed by us "hæmolytic streptococcal endotoxin," and with streptococcal exotoxin (Dick toxin), were performed on all the patients in the ward. It was found that these children gave fewer positive Dick reactions than did normals. When tested with the endotoxin, however, 100% were found to react, as opposed to 20% in a control group.

Since these initial experiments, a much larger series of rheumatic children and controls have been tested with this "endotoxin" or extract. Time does not permit me here to go into the matter more fully, except to say that the initial results reported here have been broadly confirmed, and a definite correlation found between the time which has elapsed since an attack of acute rheumatism and this hypersensitivity to the "endotoxin."

These observations at the Cheyne Hospital confirmed Schlesinger's finding of the silent period in rheumatic relapses, and showed that the organism associated with the throat infection was a hæmolytic streptococcus. They suggested a definite ætiological association between hæmolytic streptococcal throat infection and subsequent rheumatic fever. It was at once argued, however, by Warner and others, that the hæmolytic streptococcal infection was probably a non-specific factor, and that any other acute infection which might lower the patient's resistance would have the same effect. Careful study during the last year, at both the Cheyne Hospital and Queen Mary's Hospital, Carshalton, does not favour this argument. Dr. Sheldon's ward in the Cheyne Hospital has been kept under close observation and the throat flora charted week by week. By this means it has been possible to observe the effects of a number of infections occurring in the ward. These have been associated

with hæmolytic staphylococci, *Micrococcus catarrhalis*, Pfeiffer's bacillus and pneumococci, as well as the hæmolytic streptococci, while *Streptococcus viridans* and indifferent streptococci have been present throughout. Relapses have occurred only after infection with the hæmolytic streptococcus.

BACTERIOLOGY OF RHEUMATIC RELAPSES.

Organism	No. of cases with nasopharyngeal infection	No. of subsequent relapses
Hæmolytic streptococcus ...	32 ...	24
Pneumococcus	10 ...	0
M. catarrhalis	12 ...	0
B. influenzæ	12 ...	0
"Colds"	5 ...	0

Streptococcus viridans present in 90% of the throats.

In the table above it will be seen that 24 relapses of acute rheumatic fever occurred out of 32 cases showing clinical nasopharyngeal infection with the hæmolytic streptococcus. None of the other infections were followed by relapses. The *B. influenzæ* group was particularly striking. This infection occurred in epidemic form in a ward containing convalescent rheumatic children of the relapsing type. It was of a very virulent nature, resembling the epidemic of influenza in 1918, the fever in the cases affected often reaching 104° F., and lasting from four to seven days. These patients were closely observed for a month following the epidemic, but no subsequent rheumatic symptoms developed. If, then, the hypothesis that any acute infective condition may lead to rheumatic relapses was correct, we should have expected to see rheumatic sequelæ occurring after such a virulent infection.

While we were making our original observations at the Cheyne Hospital, Coburn's monograph appeared (in January, 1931), in which he sets forth a formidable array of facts in support of the view that the hæmolytic streptococcus is the infective agent in what he calls the "rheumatic state." His bacteriological findings are similar to ours, in that it was only during infection with the hæmolytic streptococcus that he observed rheumatic disease. We cannot but feel, therefore, that the hæmolytic streptococcus plays more than a non-specific rôle in the production of the disease.

Another criticism made is that we were dealing only with subjects already rheumatic and liable to relapses, and that our work is therefore no proof that primary attacks of acute rheumatic fever are caused in a similar manner. Lately, Glover and F. Griffith, while discussing tonsillitis caused by the hæmolytic streptococcus occurring in epidemics in public schools, described, as one of the sequelæ, rheumatic fever occurring from ten to twenty days after recovery from the tonsillitis. Dr. Bradley will presently describe these epidemics in schools.

Recently I have observed an epidemic of acute tonsillitis associated with hæmolytic streptococcal infection in an institution containing 600 nurses and ward-maids. Exact figures of the number of cases involved could not be obtained, but the epidemic was widespread and probably affected not less than 100 of the staff. Among the complications which followed the epidemic was that of rheumatic fever. In three of these cases, whose full particulars I have to hand, the silent period was nine, twelve and twenty-one days respectively, and all three developed carditis. Throat swabs were examined from two, both yielding hæmolytic streptococci, and all three were subsequently found to be highly sensitive to hæmolytic streptococcal "endotoxin."

It would appear, then, that there is no essential difference in the ætiology of primary and secondary attacks of rheumatic fever.

If a virulent hæmolytic streptococcal infection attacks a ward in which rheumatic subjects are congregated, a large number of secondary attacks will occur, while the same infection occurring among apparently healthy children will only be followed by acute rheumatism in patients in what we may call the pre-rheumatic state. In this

connection one of the adult cases in the last epidemic referred to is of considerable interest.

Case 2.—Girl, aged 18 years: Previous to work in hospital had lived on an isolated farm in the country. On February 2, 1931, complained of sore throat and was warded for one week with acute tonsillitis. She recovered completely, but on February 21, 1931, a second attack of acute tonsillitis developed, accompanied by vague pains in the back and limbs, vomiting, and high fever.

During the next seven days the throat gradually cleared up and the temperature fell to normal. On the ninth day the temperature again rose and the patient rapidly became very ill, the signs of a rheumatic pancarditis rapidly developing. At no time was there any arthritis.

I examined the throat some weeks after the carditis had commenced, and found the tonsils showing signs of recent acute infection being still ragged, swollen and injected with pus in the crypts. Cultures still showed the presence of large numbers of hæmolytic streptococci. Although very very ill at the time, she gave a positive reaction to an intradermal test with hæmolytic streptococcal "endotoxin." After six months' illness she died from heart failure. Blood cultures during the most acute period were sterile.

Two points are of outstanding significance in this case: (*a*) Although occurring in an adult, the rheumatic attack was of the type usually met with in children before puberty; (*b*) the tonsillitis which preceded the acute rheumatic carditis was the second attack within a month. The fact that previous to her employment in the hospital the patient had lived in the depth of the country, where it is improbable that she had been exposed to the infections met with in town communities, explains the child-type of reaction to the infection. The second point strongly supports the "allergic" hypothesis of acute rheumatism as advanced by Swift in many of his publications. It would suggest that the first attack of tonsillitis had sensitized the patient, changing her type of reactivity to infection.

The ætiology of rheumatic fever can only be explained when its connection with acute sore throat caused by the hæmolytic streptococcus is understood. It cannot be described as a contagious disease in the ordinary sense of the word, as more than one factor is responsible for its development. The streptococcal throat infection is no doubt contagious in the epidemic sense, but is only followed by rheumatic fever in certain patients. Although there is some evidence in support of the view that before rheumatic fever can develop in an individual, that person must have been previously in a pre-rheumatic condition, characterized by a changed tissue reaction to the organism or its products, this hypothesis must for the present be considered unproven.

Time does not permit me to enlarge on the possible lines which treatment may take, but they may be briefly summarized as follows:—

(A) *The Prevention of Relapses in already Rheumatic Patients.*

(1) By sufficient bed-spacing, cross-ventilation of wards, and abundance of fresh air.

(2) By the control of infection in the ward. The time is not far distant when all wards for rheumatic children will have available proper bacteriological investigation. Thus the swabbing of the whole ward when throat infection occurs will be possible, and the proper isolation of all infected patients, nurses and ward-maids will be insisted upon.

(3) By the administration of aspirin from the commencement of the naso-pharyngeal infection (Dr. Schlesinger's method).

(4) By desensitization of patients attending rheumatic clinics (Swift's method of intravenous vaccination with hæmolytic streptococci).

(B) *The Prevention of Acute Rheumatism in Normal Communities.*

(1) By the realization of the importance of throat infection, so that isolation of infected cases becomes a routine.

(2) By the elimination of over-crowding, which is the most important factor predisposing to the spread of droplet infection.

In conclusion, I should like to pay a tribute to Dr. F. Griffith, whose technique and methods have alone made this work possible, and whose encouragement and critical insight have been an inspiration to us all.

Dr. W. H. Bradley: I propose to deal with the significance and prevention of precursor fever in the rheumatic state. "The greater the improbability, the more rigid should be the proof." With these words Professor Okell [1], quoting from Hume's "Book of Miracles," has recently dismissed the hypothesis that certain pathogenic streptococci engender acute rheumatism. I have the same thought in my mind as I proceed to extend the trail which Dr. Collis has blazed for us and attempt the proof of our theorem that acute rheumatism is a manifestation of an abnormal tissue response to transitory contact with streptococci of various types.

These upper temperature charts (fig. 1) are from cases of three boys who, about February 7, of this year, contracted sore throat due to a known type of hæmolytic

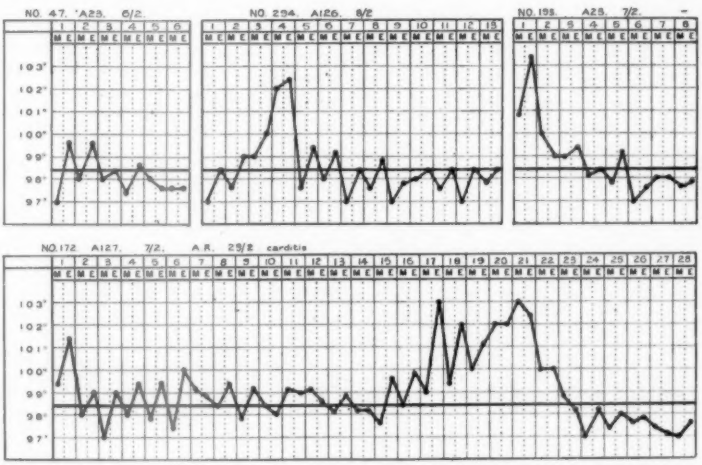

FIG. 1.—Streptococcal sore throat of same serological type occurring at same time and followed by acute rheumatism and carditis.[1]

streptococcus, the same organism being found in every throat during the first twenty-four hours of fever although it had been absent a few days previously. The charts represent a normal reaction to a new and acute nasopharyngeal infection in healthy subjects.

The lower chart is from another case of the same hæmolytic streptococcal sore throat occurring at the same time in a healthy boy, who previous to the onset of this fever was not carrying this type of streptococcus. The primary pyrexial reaction to

1 EXPLANATORY NOTE FOR CHARTS (FIGS. 1, 2, 3).

N. = Nasopharyngitis without pyrexia.
A. = Pyrexial nasopharyngitis.
1. = Coryza.
2. = Sore throat.
3. = Sore throat with exudate.
6. = Laryngeal cough.
7. = Catarrhal signs in chest.
A. R. = Acute rheumatism.

invasion of the nasopharynx appeared to be normal, but he remained under observation on account of bronchitis due to the same organism. Fifteen days after the onset of that disease acute rheumatism developed. In this chart will be recognized the lag, or silent, period which has been emphasized by Campbell and Warner [2], and Schlesinger [3], and which is most easily observed in scarlatinal rheumatism [4, 5], merely because a rash calls our attention to a hæmolytic streptococcal nasopharyngitis and we keep the patient under observation.

A further series of charts (fig. 2) are taken from cases of boys with the same type of sore throat, occurring about February 17, 1932, during the same epidemic. Boy No. 145 reacted normally to the infection and passed out of observation. Eighteen days later he developed polyarthritis, and sixteen days after that, an acute carditis. The lag period, so obvious in this chart, is typical of acute rheumatism. I suspect that it is present in every case but is not always recognized, because the original infection may be silent or, perhaps, produce but a mild apyrexial coryza. The first spike in the

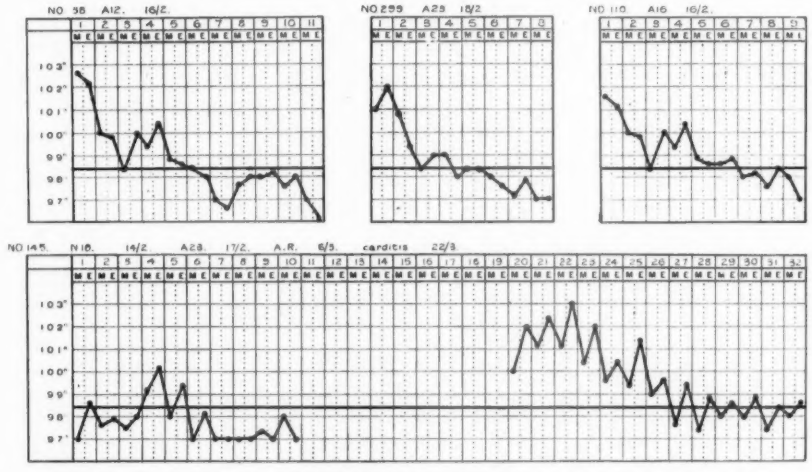

FIG. 2.—Sore throat of identical serological type occurring on same day and followed by acute rheumatism and carditis. First attack.

typical temperature chart is the salient point in the course of acute rheumatism—the salient at which our attack on the disease must be hurled.

There was reasonably rigid proof in the examples I have demonstrated that this original infection was a simple, acute, hæmolytic streptococcal nasopharyngitis communicated by droplet spread. I have observed about twenty first attacks and relapses of acute rheumatism in which an acute infection with hæmolytic streptococci, epidemic at the time, was proved to be the cause of the prodromal sore throat. The responsible organisms were of four distinct types, in three of which Dr. Griffith was able to confirm serological typing by agglutinin absorption tests, and I am certain that there is no type specificity about rheumatism, producing sore throats—except in a limited epidemiological sense, dependent on time and place.

The following charts (fig. 3) illustrate my point. They are from the case of a boy (No. 278) who suffered the first attack in February, 1930, and relapsed in March, 1932. The prodromal sore throats are indicated in the charts; the organisms responsible differed in the two attacks. I have had bacteriological proof of this phenomenon in

three other cases of relapse. Lloyd Jones [6] has suggested that the disparate findings of the bacteriologists, far from invalidating the infective theory, are accounted for by an allergic hypothesis, and allergy is a moderately satisfactory explanation of the lag period.

Clinically, acute streptococcal nasopharyngitis is strongly implicated as the main allergizing factor in the rheumatic state. Equally strong arguments in proof of our theorem arise out of the epidemiological studies which Dr. Collis has surveyed in some detail. Viewing the matter from a slightly different angle and in a more general way, I propose to consider three masses of people: (1) The population at large; (2) the semi-isolated community; (3) the semi-isolated community of rheumatic susceptibles.

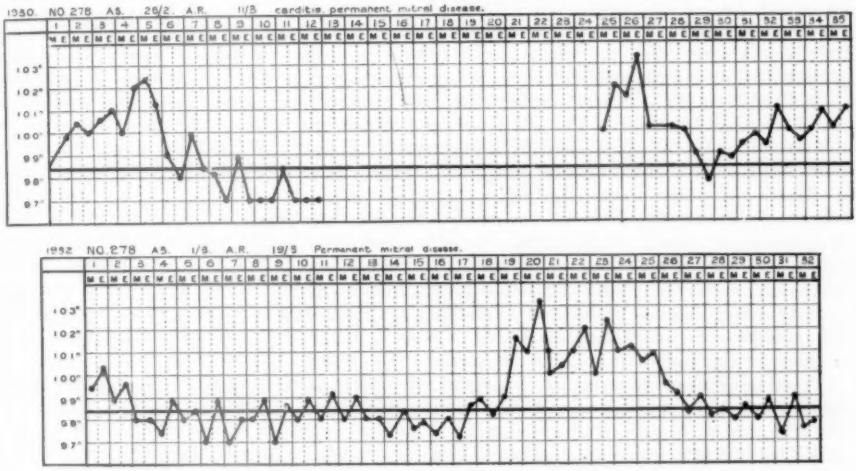

FIG. 3.—Relapse of acute rheumatism with serious deterioration of heart. Prodromal sore throat observed on both occasions. Type of hæmolytic streptococcus varied on each occasion but was identical with type known to be epidemic at the time.

Acute rheumatism in the general population appears to be a family disease [7, 8, 9, 10, 11, 12], and occasionally its incidence in a house assumes epidemic proportions [13, 14, 15, 16, 17, 18]. Intimate study of family incidence has caused Paul [19, 20] to write: "Recurrent activity of disease seems to sweep through a family in synchronous waves, during which time new cases may also appear . . . accompanied by the simultaneous appearance of non-specific types of illness such as bronchitis, broncho-pneumonia, skin rashes, etc., in other members" . . . of the household, suggesting a common nasopharyngeal cause.

Rheumatic families are frequently concentrated into rheumatic localities, the rheumatic morbidity in any given locality appearing to increase in proportion with density of population and dampness [21, 22, 23, 24, 25], and frequently to follow the course of waterways [26, 27]. The recent Bristol investigations, to which Dr. Carey Coombs will refer, show, however, that the attack rate of rheumatism in Bristol is five times [28] as great as in the neighbouring city of Bath where the incidence appears to be falling [29], in spite of the fact that the Bath slums are over-crowded, situated near a river, frequently flooded, and notoriously humid. A factor not perceptible to the naked senses would appear to be at work.

Other observers, e.g., Monnier, Andrieu [30], favoured by the locality in which they practised, have reported distinct epidemics of rheumatism spreading from village to village, and marked periodic increases in incidence in the open population have been recorded from time to time [31, 32, 33, 34, 35] 36, 37, 38] not infrequently associated with waves of known streptococcal disease [39, 40].

The semi-isolated community provides material for a more intimate study, and many epidemics under such conditions have been recorded [42, 43, 44, 45, 46, 47], some of which have recently been considered by Glover [48, 49], who writes, "In acute rheumatism epidemics an 'unseen' carrier wave is probably present, but in addition there are two visible waves—the larger tonsillitis wave and the smaller acute rheumatism wave."

In Michaelmas Term, 1929, a junior school of ninety boys was involved in an extensive spread of hæmolytic streptococcal tonsillitis, producing four cases of rheumatism. At this time the upper school (240 boys) was comparatively healthy. In the following term the order was reversed, the upper school suffering a serious attack of sore throat, with ten cases of rheumatism, while the junior school remained free except for two cases—one the brother of an upper school boy, also involved, and the other a relapse. The only variants in the environment of these two groups of boys are those associated with personal contact. From that time onwards complete bacteriological control has been kept by Dr. Griffith. In Lent Term, 1931, a new type (Hutchinson) of streptococcus invaded the school and produced rheumatism. A third wave occurred later, another distinct type of hæmolytic streptococcus being responsible. Acute rheumatism appeared when expected, i.e., after the peak of the tonsillitis wave. Previous to 1929, wave after wave of nasopharyngitis had swept the school, with never a case of rheumatism. I observed three such epidemics, in two of which pneumococci were responsible. In the third *Streptococcus viridans* was a possible cause. Hæmolytic streptococci had been rare visitors to the school before the appearance of rheumatism-producing sore throats.

In most closed community epidemics reported, the morbidity from rheumatism has exceeded the highest attack rate in the open population. Yet, when a streptococcal nasopharyngitis invades an isolated community of rheumatic susceptibles, the attack rate is far in excess of that in a healthy closed community. Dr. Collis has told us of those epidemics in cardiac hospitals in which bacteriological control was available and it is reasonably fair to assume a streptococcal origin for the basic wave of upper air passage infection which produced 10% relapses of rheumatism in Boas and Schwartz's two epidemics [51], and 25% in that observed by Hillier and Graef [52]. Hector [53] states that of all scarlet fever cases admitted to an isolation hospital, 0·55 % only produced rheumatism or cardiac symptoms, but in cases with a previous history of acute rheumatism there was 100 % reappearance of the symptoms associated with the rheumatic state.

The rheumatic subject would appear to be at the mercy of certain nasopharyngeal diseases whereby his relapses are precipitated. Is this association merely accidental, or has it an important etiological significance? Epidemiologically there is no doubt that acute rheumatism has the characters of an acute infectious fever and is immediately related to certain types of epidemic sore throat. Clinically there is equally little doubt of the truth of Millar's [25] dictum: "Direct infection from one case to another is of no practical importance," and the great frequency of the apparently sporadic case unassociated with any epidemic makes it difficult to believe the epidemiological evidence.

Our theorem provides a link between these two incompatible truths. The precursor fever is that link. It is highly infectious, its infectivity diminishes rapidly during the lag period, and the infecting organisms are not necessarily present in the nasopharynx at the time of onset of arthritis. Furthermore the precursor fever will produce rheumatism only in certain hypersensitive subjects. The work of Collis and

Sheldon goes far to show the nature of this rheumatic susceptibility and, if allergy is the prime factor in rheumatism, surely a series of acute contacts with the allergen —believed to be streptococcal endotoxin—will best serve the conditions required for the development of an allergic state,

Broadly speaking we are back to Newsholme [54] who, in his Milroy lecture of 1895, presumed a threefold cause of rheumatism: (1) an acute infective agent; (2) the environment; (3) a personal factor.

This triad will serve us well in a discussion of the prevention and treatment of the disease. The personal factor, so strongly suggested on epidemiological grounds, may be amenable to those methods of immunization and desensitiation which Dr. Collis is testing. The environment, maleficent in proportion to density of population, humidity, and season, is just that environment in which droplet infections most easily spread, but it must include an essential factor described by Coburn [55], namely a widespread streptococcal parasitism. The acute infective agents become almost ubiquitous at certain times and in certain places. Although they can—and do—exist in other parts of the body, their main habitat is the surface of the nasopharynx whereon they are merely temporary residents (except in rare cases of chronic infection) and whence they are disseminated, most commonly by droplet spray. It may be that, in rheumatism, their residence is more permanent, but this has yet to be proved. They spread slowly, causing sub-epidemic states rather than steeple-like epidemics, and they are frequently carrier-borne [56, 57, 58, 59, 60, 61, 62, 63). They commonly produce follicular tonsillitis as a physical sign, but sore throat or simple coryza, with or without pyrexia, may mark their attack.

Such attacks are the "precursor-nasopharyngitis" which, after a lag period, engenders rheumatic fever—itself not necessarily an infectious disease.

Of the treatment of this allergizing sore throat I have little to say. Continuous administration of aspirin from the onset of nasopharyngitis, as advocated by Sheldon [64], appears to be of value and should be carried out; prophylaxis offers much greater hope. Tonsillectomy in the prevention of rheumatism is a lost cause [55, 65, 66, 67] and certain well controlled studies have shown it to offer no appreciable degree of protection against simple acute nasopharyngitis [63, 68, 69]. Our problem is rather to reduce the spread of droplet infections—*all* droplet infections, because clinically we cannot, with certainty, distinguish one from another.

In closed communities the isolation of acute catarrhs may be possible but is rarely effective. In the population at large it is clearly impossible to obtain adequate control of all carriers, well or ill. Dr. Collis and other workers [70, 71] have demonstrated the possible value of skin tests for rheumatic susceptibles, who, when detected, must be taught to insulate themselves against droplet infection.

There is one insulating material which recommends itself above all others—namely, fresh air—and an abundance of this material must be used in the treatment of rheumatics. Coburn's well-known Porto Rico experiment is a probable example of the value of this method and Dr. Gray Hill [72] speaks well of it.

In rural areas continued rest in a home chalet should be enjoined. The less fortunate town dwellers should be housed in single bedrooms with wide-open windows, unless it is possible to move them to the chalet type sanatoria. The institution in which rheumatism occurs frequently should be wide-spaced and divided into small communities.

The cardiac hospital, so valuable for its routine of rest and graduated exercises, is not altogether an unmixed blessing when sore throat invades it, and I would warn you against over-rating the value of isolation in the control of this trouble. Efficient insulation is much safer, although immediate isolation of all cases of nasopharyngeal disease must still be practised. Other points of importance are a well mixed diet with a full ration of vitamins—particularly vitamin "A," nasal breathing, a useful skin reaction, warm feet and a cool head. Clean handkerchiefs and a hand covering

a coughing mouth are all directed to the same end, namely, that the pre-rheumatic and the rheumatic must not "catch cold."

Summary and Conclusions.

1. The typical first attack or relapse of rheumatism includes:—
   (*a*) An acute reaction, most commonly with involvement of the upper air-passages referred to as "precursor fever" in this paper, which is followed by (*b*) A lag or silent period preceding (*c*) The classical manifestations of polyarthritis and carditis, or a state of toxic debility.

2. Search of the literature shows that acute rheumatism occurs in association with epidemics of tonsillitis and nasopharyngitis.

3. Hæmolytic streptococci of various types are shown to cause: (*a*) The precursor fever. (*b*) Epidemics of rheumatism producing tonsillitis.

4. Droplet infection appears to be the main mode of spread of hæmolytic streptococci. A widespread streptococcal parasitism is an essential factor in a rheumatic environment.

5. The precursor fever is due to acute and transitory infection with streptococci. Rheumatism appears to occur in those who, being incompletely immunized by a first contact, with a rheumatism-producing streptococcus, develop a hypersensitiveness (allergy) to that organism. Subsequent contact with allergen (endotoxin) precipitates rheumatism.

Control of rheumatism requires the prevention of the precursor fever. Among therapeutic and prophylactic methods, the value of fresh air must be emphasized.

Acute rheumatism is a manifestation of abnormal tissue-responses to acute and repeated contact with streptococci commonly spread by droplet infection. The problems of the rheumatic state are the problems of the simple acute nasopharyngeal diseases.

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Dr. Carey F. Coombs: The observations which we have been making in the Bristol district during the past few years furnish an interesting background to the facts brought forward by Dr. Bradley. We collected, during a period of three years, reports on all cases of rheumatic heart disease in children between the ages of 5 and 14 years, within the area embraced by the counties of Gloucestershire, Somerset and Wiltshire. The outstanding fact that emerges from this inquiry is graphically presented in a map which Dr. Perry has kindly prepared for me, namely, that the incidence of the disease per 1,000 of the population was five times as high in Bristol as in the surrounding country area. Further, a scrutiny of the country area reveals no single environmental favouring factor of importance. The Bristol map has yet to be scrutinized.

It was in this unfavourable area that the outbreak described by Dr. Bradley occurred, and at about the same time I saw similar, but less impressive, outbreaks in an industrial school in another part of Somerset. Neither on the background of geography, nor, certainly, on that of unfavourable domestic conditions, can these outbreaks be explained in terms of environmental factors. In passing, one may perhaps note that these factors might be adduced by way of explaining both the small percentage of those with bad throats who developed rheumatism, and the benign course which these followed. Yet even these facts might also equally be ascribed to the good resistance which these boys would be expected to put up.

Now, which explanation can be used to account for the prevalence of the infection in Bristol as compared with that in the surrounding country? In parenthesis, I may say that steps are being taken to see whether rheumatism is so predominant a factor in the causation of cardiac disease elsewhere in Britain, and—I hope I may say—in Europe. All that can be said so far, however, is that we have tested our figures as well as we can, and they appear to be valid. I do not think we can go far with any attempt to explain them, but Dr. Herbert Rogers is undertaking some bacteriological investigations of which he says: "A series of swabs from the tonsils have been taken, at intervals of about one month, from children having definite evidence of rheumatic carditis, and from children having no signs of this disease. There appears to be little difference in the bacteriology of the two series. Ninety per cent of the total number of swabs contain streptococci. The majority of these streptococci are inert to fresh blood agar, i.e., are neither hæmolytic nor of the *viridans* type. Hæmolytic streptococci seem to be rare and do not form 5% of the swabs taken. The *viridans* type becomes more prevalent in the Spring months in both rheumatic and non-rheumatic children. Environment (i.e., Bristol General Hospital and Winford Hospital) does not seem to affect the bacteriology of the throat during nine months."

These inquiries by Dr. Rogers are being paralleled by other investigations at Gloucester, undertaken by Dr. Davey, and we hope something will come of them. In the meantime, there can be little doubt that urbanization, with all that it implies, is, in our area at all events, a powerful factor in the perpetuation of cardiac infection, and this furnishes a strong argument in favour of the country hospital.

We have made a beginning with this plan at the Winford Hospital, about five miles from the centre of the city. It is primarily an Orthopædic Hospital, in which we are allowed about twenty beds. We hope to have a block of about fifty beds for

the cardiac cripples before long. As we have a system of clinics at work through the area of the three counties, there is never any lack of cases ; indeed, we could fill the fifty beds at any moment. As far as we have gone, our observations show that while the children are under treatment in the hospital they do well, but that there is a regrettable tendency to relapse on their return to their city homes. There have been one or two cases in which the period of lag between tonsillar infection and rheumatic recrudescence has been noted, as at West Wickham. I ought not to say more about this or about observations in progress, but I feel sure, with Dr. Collis, and with my colleagues Drs. Herapath and Perry, who are in charge of the Winford children, that this continuous observation over long periods will, as Dr. Poynton has foretold, yield much valuable knowledge as to the natural history of the disease.

Section of Odontology.

President—Mr. E. B. Dowsett, D.S.O., L.R.C.P., M.R.C.S., L.D.S.E.

[*March* 21, 1932.]

Some Clinical Observations in connection with the Causation of Deformities of the Dental Arches.

By J. G. Turner, F.R.C.S., L.D.S.Eng.

There are three points to which I want to draw attention in this paper :—
(1) The movements of teeth in the jaws, as revealed after extractions. (2) Movements due to forces external to the bone. (3) The association of deformity with "adenoids."

As far as possible I will deal with them separately.

(1) *Movements of teeth in the jaws, as revealed after extractions.*—These movements must not be confounded with the general forward movement of the dental arch with the body of the bone (maxilla or mandible), which accompanies, and is part of, the development of the face. Like this general forward movement of the bones, these special tooth movements are confined to the growth age, but they differ markedly in the two bones.

(*a*) In the maxilla it is well known that if $\frac{e}{5}$, 6 or 7 be extracted in early life the posterior teeth come rapidly forward ; in the body of the bone if they are not yet erupted. The movement depends on active bone growth, and as I shall show later, tends to be in abeyance when bone growth fails.

If an upper $\frac{d}{4}$ be extracted early, the general opinion seems to be that the same forward movement of the posterior teeth follows. This, however, is not the case. So long as $\frac{e}{5}$ is in position there is no forward movement of the posterior teeth. The $\frac{e}{5}$ makes an absolute block (figs. 1 and 2).

(*b*) In the mandible the general opinion is that a similar forward movement takes place. But, in fact, no such movement obtains. If a lower $\frac{e}{5}$, 6 or 7 be extracted early, the posterior teeth will tilt forward, or if unerupted, will erupt in the axis of the developmental position. But my point is that if a lower 6 be extracted early, the 5 and, to a lesser extent, the 4 and the more anterior teeth, will travel back. The 5, if unerupted, will travel back in the body of the bone and may erupt hard against the 7. This movement is comparable to the forward movement of the

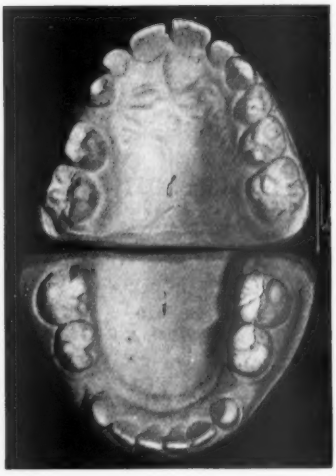


FIG. 1.—Models showing early extraction of $\frac{d\,|}{d\,|\,d}$. There is no forward movement of the posterior teeth.

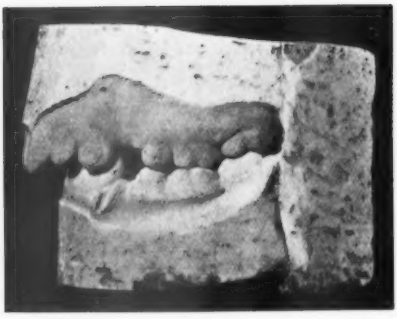


FIG. 2.—Models (Adult). All 4's were extracted in early youth for regulation. There is no forward movement of the posterior teeth + or −.

FIG. 3.—X-ray pictures of mandibular cheek teeth showing the tilting of the 7 after extraction of 6, which is commonly mistaken for forward movement. The gap between the root apices of 7 and 5 shows that the apposition of the crowns is only due to tilting.

upper molars; it is a movement of the whole tooth. The fact that after early extraction teeth become tilted towards the vacated socket has led to the idea that, e.g., the lower 7 moves forward just as an upper 7 does, and Sir Norman Bennett figures a case in which he asserts that this has happened. He, further, cannot understand how 5 could move back against the interlocking bite. But he has overlooked two important points (there are others, i.e., both ± teeth are pushed back, and − teeth may move in a groove formed by the cusps of the +). To prove his case he must show an X-ray picture with the roots of 5 and 7 close to and parallel to each other: such a skiagram is very hard to obtain—I have only one and the bite shows that the lower 7 retains its normal position while the upper 7 has moved forward; i.e., the anterior teeth have gone back. Far more often the backward movement of 5 has not been rapid enough to reach 7 before this has tilted and an X-ray picture shows crowns in apposition, but a wide gap between the root-apices (fig. 3). The other point he has missed is that 5 goes back in the body of the bone. Presumably it can be stopped by intercusping, but unless that occurs, if a lower 7 be extracted early the 5 will move back. If now a lower $\frac{d}{4}$ be extracted early, the lower $\frac{e}{5}$ remains steady, it has no tendency to move forward any more than has the upper $\frac{e}{5}$ (see figs. 1 and 2).

During the growth age there would seem to be currents of bone at work in the bodies of the bones. The current in the maxilla sets forward and is blocked by $\frac{e}{5}$, and probably, so far as I can judge, never reaches 4.3.2.1. The current in the lower sets backward and is most intense in the 5 region: it can and does affect 4.3.2.1, and I have shown some cases suggesting that it affects 6.7.8. (The developmental position of 6.7.8 necessitates a backward rotation to allow of eruption.)

(2) *Movements of the teeth due to external forces.*—These movements again are best shown by the results of early extractions. They cease with adult life when the bones are hardened. For convenience, we may divide them into: (*a*) tilting movements; (*b*) compression movements.

(*a*) Tilting movements, by which I mean the tilting of a tooth towards a vacated socket, are generally explained as being due to the action of biting, and though I am not satisfied with the current diagrams of the resolution of forces, I have to acknowledge I can find no other explanation, except possibly the action of the buccinator. For my purpose to-night they are of importance because, as I have already shown, the forward tilt of the lower 7 gives rise to the idea of a movement forward *in toto*.

(*b*) Compression movements. These are important because they show the compressing power of the lips and cheeks. They are well shown by the results of early extractions, and, again, they cease in adult life when the bones are hardened.

As a general description one may say that whenever in early life a member of the dental arch is extracted, the remaining teeth tend to be pushed together till they are in stable apposition. The movement of any individual tooth may be only a tilting, i.e., a swing from the apex, but appearances often suggest an absolute flattening, including the whole of the alveolar bone. These movements are the invariable accompaniment of early extractions and are of importance from an ætiological standpoint because there is no other factor which can account for them except the compressing action of the lips and cheeks (see fig. 6, p. 64).

It has been objected that, at most, the lips and cheeks can exert but a slight force of compression, but, in fact, only a very slight force is needed for the purpose, as every orthodontist knows, especially when the teeth are still but partly formed and the sockets wide-mouthed. I believe it is agreed that Darwin was right in attributing the change of direction of the auditory meatus of the lop-eared rabbit to the

drag of the lop-ears: I have never weighed the lop-ears, but they cannot be very heavy and their effects are very far-reaching. But there is direct clinical proof of the compressing action of the lips and cheeks to be found in those rare cases of early unilateral facial paralysis.

Dr. Lack has recorded one in his book on "Diseases of the Nose," Mr. J. S. Barr has recorded one in the *British Dental Journal*, 1910, xxxi, 483, and I myself found one in the asylum at Waddesley Bridge, Sheffield. In these cases the dental arches, both upper and lower, are undistorted on the paralysed side, but flattened on the active side. Obviously, muscular action cannot be put out of count in these cases, though they were all adenoid cases and mouth-breathers, and the possibility of additional compression action by the stretched tissues of normal tone must be considered. The tissues of the cheeks, and especially the muscles, are all normally elastic, and the open mouth may well bring this force into play. There is, indeed, clinical evidence that this occurs. It is actual clinical experience that it is useless to expand the dental arches while mouth-breathing persists; as soon as the apparatus is taken away the compression deformity recurs. It is also clinical experience that success can be attained in these cases when the mouth-breathing is cured.

(3) *The association of deformities of the dental arches with adenoids.*—Statisticians are demanding of us figures to prove a significant correlation between adenoids and deformities of the dental arches. I am sorry I have none, but clinically there is a most significant correlation. During the last year I have only found, in my work at the Royal Dental Hospital, London, two cases in which there was not an appreciable amount of adenoids present, and in both these cases there were large tonsils. I may say that I rely on a throat specialist for the diagnosis. Further, I find that I can diagnose the presence of adenoids, almost to a certainty, by the condition of the dental arches. To do this it is necessary to remember that there are two deforming factors in adenoid cases: (*a*) Failure of growth of the maxilla. (*b*) Lateral compression.

Failure of growth, I find, accompanies even a small adenoid pad, such a pad as apparently leads to no mouth-breathing. In adenoid patients with broad naso-pharynges, failure of growth of the maxilla is common while compression deformity is rare.

In the patients with narrow naso-pharynges, both growth-failure and compression are at work, and compression may begin so early as to deform the temporary arches.

Failure of growth is evidenced by persistence of a developmental stage belonging to an earlier age. It may begin as early as the period of eruption of the temporary incisors. In this case these teeth will retain some degree of their developmental positions. Instead of conforming to a regular arch, they will present some degree of the position shown in the diagram, which is their developmental position $\frac{\text{lip}}{\text{tongue}}$.

Later, the temporary incisors and canines should be found well spaced, e.g., at $4\frac{6}{1\,2}$. Failure of spacing I have found a most valuable clinical sign of adenoids.

On the eruption of the permanent teeth, persistence of the developmental positions of the laterals and canines is a marked feature. The laterals are usually developed inside and partly behind the centrals (sometimes the developmental position is labial to the centrals) and this is the position in which they are found in the deformed arches we are considering; sometimes they are found almost meeting in the mid-line, a position best explained as an accentuation of the developmental position by external compression. The canines are developed above the rest of the teeth, 4 and 2 being almost in contact, and in the cases we are considering, this is their position of eruption. There has never been sufficient bone growth to accommodate the canines. When they erupt, they at once come under the compressing action of the cheeks and the apparent protrusion of the upper incisors often becomes accentuated. It will be recalled that the conditions above noted as occurring in the maxilla are often found

simultaneously in the mandible—because the lower arch is included in the upper, not because of subnormal growth of the mandibular body.

There is further clinical proof of the correlation of failure of maxillary growth with adenoids in the fact that removal of the adenoids is followed by an almost sudden resumption of maxillary growth. It is often possible to date the age of adenoid operation by noting a sudden widening of the arch, in the region, e.g., of the

FIG. 4.—Showing widening of the upper dental arch in 6 region after operation for adenoids at age of $4\frac{6}{12}$.

FIG. 5.—Showing widening of the upper dental arch in 7 region after operation for adenoids at age of 10.

6, which suggests a date before the age of $5\frac{6}{12}$ (fig. 4). On the other hand the patient who has been left without operation will show an arch narrow in its whole length or one that widens in the 8 region as he "grew out of his adenoids" (fig. 5).

Another clinical observation I have made is that even the forward movement of the upper 6's and 7's—a movement which with normal growth is surprisingly active—may be almost in abeyance in the presence of adenoids (fig. 6, p. 64).

It is very important to note that lost growth is never made up for, and that the longer the adenoids persist, the worse will be the deformity of the dental arches.

To prevent confusion of thought, I may add that I am not maintaining that every deformity of the dental arches is accompanied by adenoids. I do maintain, however, that by far the majority are, and that early removal of the adenoids will prevent

FIG. 6.—Unoperated adenoids. Early extraction of $\underline{6}\,|$ has been followed by no forward movement of $\underline{7}\,|$ (X-rays show it is tilted forward); $5 \cdot \overline{4} \cdot 3$ have been pushed back and in by cheek-pressure. In a normal case $\underline{7}\,|$ would have moved rapidly forward.

their occurrence. And here again there is good clinical evidence, for it is my experience that since the operation for removal of tonsils and adenoids became so popular, I have seen far fewer of the extreme deformities than I saw 30 years ago. Is it permissible to add that the evolutionary explanation deprives us of all hope of prevention?

Section of Surgery.

SUB-SECTION OF PROCTOLOGY.

President—Mr. W. S. PERRIN, M.Ch.

[*March* 9, 1932.]

Ano-Rectal Fistulæ.

By W. ERNEST MILES, F.R.C.S., F.A.C.S.

THE rectum is frequently the seat of fistulous communications, which are referred to as *fistulæ-in-ano*—a bad term because it implies implication of the anus only—or as *ano-rectal fistulæ*, a much better term, expressing implication of not only the anus but the anal canal and the rectum as well. The surface apertures of ano-rectal fistulæ are located in the perineum, but it must not be assumed that every surface aperture of a fistulous track encountered in the perineum is necessarily that of an ano-rectal fistula. For instance, in the anterior, lateral and posterior regions of the perineum surface apertures may exist (fig. 1) which lead into fistulous tracks that have no connection with the rectum whatever. Thus, a surface aperture situated in the anterior part of the perineum, in or near the middle line, is probably that of a urethral fistula, the result of a peri-urethral abscess due to the presence of stricture of the urethra. A surface aperture in the lateral part of the perineum, especially when in proximity to the transverse anal line at a distance of not less than two inches from the middle line, is probably the point of evacuation of a pelvi-rectal abscess. An abscess of this kind is the result of suppuration originating in the parametrium, the base of the bladder, the prostate, or the vesiculæ seminales, and occupies primarily the superior pelvi-rectal space of Richet. The pelvi-rectal space is shut off from the para-rectal space by the fascia propria of the rectum (fig. 2), by which the pus is prevented from being discharged into the rectum. Though originally situated above the levatores ani, the pus extends through the latter and invades the ischio-rectal fossa, ultimately finding an exit through an opening upon the skin surface. Again, a surface aperture situated in the posterior part of the perineum in the middle line, between the tip of the coccyx and the anal margin, may be the point of issue of a suppurating dermoid. Such dermoids usually develop at the site of a post-anal dimple and often contain hair. When a surface aperture is situated laterally to and about an inch distant from the tip of the coccyx, especially when a second opening is symmetrically placed on the opposite side, the apertures are probably the vents of a presacral abscess. These abscesses are the result of suppuration of the presacral lymphatic glands. The pus is situated between the sacrum and the fascia propria of the rectum. The latter effectually prevents the pus from being discharged into the rectum, so that it gravitates downwards and invades the posterior part of the ischio-rectal fossa by passing through the interval between the coccygeus and the levator ani to find an exit on one or on both sides of the ano-coccygeal ligament. Lastly, a surface aperture situated close to the middle line, at the level of the upper extremity of the internatal cleft, indicates the existence of a sacro-coccygeal sinus. A sinus in this situation is generally supposed to lead down to carious bone but, so far as my experience goes, it never does, nor has it any connection with the rectum. It is the result of a hæmatoma caused by a fall upon the buttocks. The aperture leading into the sinus is almost invariably situated on the left side within half an inch of the upper extremity of the internatal cleft, a circumstance that is probably accounted for by the fact that right-handed people fall more heavily upon the left side.

With the exception of the above and also of those leading down to carious bone in the neighbourhood of the tuberosity of the ischium, the sacrum, or the coccyx, all other surface apertures of fistulous tracks found in the perineum are those of ano-rectal fistulæ.

Ætiology of Ano-Rectal Fistulæ.

Fistulous communications between the skin surface of the perineum and the interior of the anal canal or rectum are occasionally established by penetrating wounds from without, or from extravasation of fæcal material into the peri-rectal tissues as the result of perforation of the rectal wall by a carcinomatous growth or by an ulcer in the vicinity of a fibrous stricture. Such ano-rectal fistulæ pursue an atypical course which is entirely dependent upon trauma or pre-existing disease. With these exceptions every ano-rectal fistula is preceded by an abscess which is the outcome of infection conveyed to the tissues, in which the abscess forms, chiefly by means of the lymphatics.

In the majority of cases the infective process starts in a lesion situated either in the anal canal or in the lower half of the rectal ampulla. The lesions usually responsible are: a thrombosed internal pile, extravasation of blood from a ruptured vein in the submucosa, a fissure at the anal margin, a torn down anal valve, laceration of the pedicle of a polypus, an ulcerated surface in a sinus of Morgagni and puncture or laceration of the mucosa, either by small fragments of bone which have been swallowed or by the needle of a syringe employed in the treatment of internal hæmorrhoids by the injection method. There is no doubt also that occasionally peri-rectal suppuration is due to micro-organisms gaining access to the tissues by means of the blood-stream. Many years ago very opposite opinions upon this point were held by two eminent contemporaries, Sir Benjamin Brodie and Mr. Syme, both of whom evidently entertained a leaning towards proctology. Brodie confidently asserted that fistula-in-ano was due to the existence of an ulcer in the mucous membrane, and that the suppuration in the neighbouring tissues was subsequent to and dependent upon the ulceration. Mr. Syme, on the other hand, asserted with equal confidence that the inflammation and suppuration took place in the tissues external to the bowel and that the abscess subsequently opened into the rectum. No doubt Mr. Syme was mindful of the prevalence of ischio-rectal abscesses among carpenters and stone-masons from sitting upon damp and cold seats, and among cavalrymen from riding upon wet saddles. Nowadays, by the aid of blood-cultures, we know that micro-organisms circulate in the blood-stream under certain conditions and, finding a suitable nidus in low resisting fatty tissue, may give rise to suppuration. Just in the same way as a perinephric abscess may result from staphylococcic infection originating in a suppurating furuncle of the scalp, so may an ischio-rectal abscess be consequent upon dental pyorrhœa or other distant septic focus.

The sequence of events, therefore, leading up to the establishment of an ano-rectal fistula is, in the majority of instances, as follows: (*a*) Appearance of an initial lesion; (*b*) septic lymphangitis or phlebitis, as the result of infection by micro-organisms; (*c*) suppuration eventuating in the formation of a localized abscess; (*d*) evacuation of the pus either into the bowel or through the skin, or in both situations, thus giving rise to (1) an incomplete, or (2) a complete fistula.

Classification of Ano-Rectal Fistulæ.

It is usual to divide ano-rectal fistulæ into three varieties: (*a*) the *complete fistula*; (*b*) the *blind external fistula*; (*c*) *the blind internal fistula.*

My objection to the above universally adopted classification of ano-rectal fistulæ is that it conveys the impression that they are varieties of a single type differing only in degree, and therefore equally amenable to treatment by the simple surgical procedure of laying open the fistulous track completely from the external opening to the internal opening and allowing the resulting wound to heal progressively from the bottom. There is no doubt that many fistulæ can be completely cured by this simple procedure, and yet it frequently happens that, when carried out in some instances, disastrous results ensue, on account of loss of control over the anal outlet.

The explanation of these widely divergent results is that there are several types of fistulæ differing in the anatomical relationship of the main track to the various muscles controlling the anal outlet. Every fistula of inflammatory origin is preceded by an abscess, and the main track of the fistula is the contracted but unobliterated original abscess cavity. The anatomical site of the original abscess, therefore, determines the type of the fistula.

The abscesses which precede fistula formation are the result of a septic focus in the terminal portion of the rectum, which extends by means of the lymphatics. The lymphatic system of the rectum consists of two plexuses, the submucous and the intermuscular, the efferents from which communicate with (1) the lymph sinus of the rectum, a space existing between the external muscular coat and the peri-rectal fatty tissue, and (2) the subcutaneous peri-anal lymphatics. The efferents from the anal canal also pass through the fatty tissue of the ischio-rectal fossa on their way to Alcock's canal. As the result of sepsis within the rectum an abscess may form in any of the above situations, and since the anatomical site of the abscess determines the type of the resulting fistula, the following classification of ano-rectal fistulæ seems to be anatomically advisable:—

(A) *The subcutaneous*
- (1) blind external
- (2) blind internal
- (3) complete

(B) *The submucous*
- (1) blind external
- (2) blind internal
- (3) complete
- (4) bilateral

(C) *The intermuscular*
- (1) blind internal

(D) *The para-rectal*
- (1) blind internal
- (2) complete
- (3) bilateral

(E) *The subsphincteric*
- (1) blind internal
- (2) complete
- (3) bilateral (anterior horseshoe)

(F) *The ischio-rectal*
- (1) blind external
- (2) blind internal
- (3) complete
- (4) bilateral (posterior horseshoe)

FEATURES OF INTEREST PRESENTED BY A COMPLETE ANO-RECTAL FISTULA.

A complete ano-rectal fistula presents four features of interest, namely: (1) The external opening; (2) the internal opening; (3) the main track; and (4) the offshoots or extensions from the main track.

(1) *The external opening.*—A great deal of information can be obtained in regard to the probable type and nature of a fistula by observing the size, position, and number of the fistulous apertures to be seen in the perineal region. As a general rule, if the opening is small and contracted, and especially if it should be situated within an inch of the anal verge, the fistula is probably subcutaneous in type. Should the opening be large, irregular in shape with undermined edges, and particularly if the surrounding skin is of a reddish-purple hue, the fistula is most probably tuberculous in origin. When the opening is surmounted by a tuft of granulation tissue such as is often observed at the orifice of a sinus leading down to carious bone, a deeply-seated fistula, such as the ischio-rectal or the para-rectal, is indicated. Should the opening be situated close to the anal verge or within half an inch of it, the fistula is invariably of the submucous type.

Lastly, the presence of several external openings is an indication of the existence of offshoots from the main track of a deeply-situated fistula, such as the ischio-rectal or the para-rectal.

Although a great many ano-rectal fistulæ have only one external opening, multiple openings are the rule rather than the exception in those of the ischio-rectal type. In these there is only one internal opening, situated in the middle line posteriorly, opposite the interval between the sphincters, and often of large size. When the internal opening is large, sometimes large enough to admit the tip of the index finger, fæcal matter is apt to enter it when an action of the bowels takes place, thus provoking acute inflammation along the main track of the fistula. As the result, then, of septic lymphangitis, secondary abscesses are formed in the vicinity of the main track. These abscesses eventually extend to the skin surface and open there, forming secondary openings. The original external opening is known as the primary opening, and indicates the termination of the main track of the fistula. Openings in connection with the same fistula which appear subsequently are secondary openings and represent the surface terminations of offshoots from the main track. It must not be forgotten, however, that external openings may not always be connected with the same fistula. It sometimes happens that two or more separate fistulæ exist in the same patient, each having a separate external opening. Instances occasionally occur in which two, three or four separate complete fistulæ co-exist in the same patient.

(2) *The internal opening* is always located in the interior of the bowel and is due to perforation of the mucous coat. As a rule internal openings are of small size and are generally circular in outline, but occasionally they are much larger and of irregular shape, as for example when they are the result of lacerations of the mucosa, such as might be produced by partial tearing through of the pedicle of a polypus, the tearing down of a valve of Morgagni, or an abrasion caused during the passage of a foreign body, such as a fish-bone. When an internal opening is exceptionally large, the fistula is usually tuberculous in origin.

The position of an internal opening varies according to the type of the fistula with which it is associated. Thus, the internal opening of a para-rectal fistula is generally situated above the level of the levatores ani, at a distance from two to three inches above the anal margin. That in connection with a fistula of the submucous type may be situated anywhere along the course of the main track, but is generally found immediately above Hilton's white line. The internal opening of a sub-sphincteric fistula is always situated in the anal canal in one of three positions at the level of the valves of Morgagni, namely, either in the right anterior quadrant or in the left anterior quadrant or in the middle line posteriorly. The internal opening of an ischio-rectal fistula is always situated in the middle line posteriorly opposite the interval between the external and internal sphincters. The internal opening of the intermuscular type may be situated anywhere in the circumference of the anal canal but always at the level of the interval between the sphincters.

In the majority of cases there is only one internal opening to each complete or blind internal fistula, but occasionally there are two. When a second internal opening, in connection with the same fistula, exists it is generally situated at a higher level along the course of the submucous track extending vertically or obliquely upwards from the lower opening. When more than one internal opening is discovered at the same level, each opening belongs to a separate fistula. If there is an internal opening at the level of the interval between the internal and external sphincters, and a second opening is found higher up without an intervening submucous track between them, both are internal openings of a para-rectal fistula.

The *position* of the external opening of a fistula, as regards the distance from the anal margin and its relation to the *transverse anal line*, is sometimes an indication to the position of the internal opening. This valuable and practical observation was

made by Goodsall, of St. Mark's Hospital, and became known as Goodsall's rule. According to his observations, if the primary external opening is situated from an inch to an inch and a half distant from the anal margin, and either anteriorly to or on the transverse line, the internal opening will be found opposite the interval between the sphincters in the same radial line as the external opening, and the main track will be straight. Secondly, when the external opening is a similar distance from the anal margin but situated posteriorly to the line, the internal opening will be found in the middle line posteriorly opposite the interval between the sphincters, and the main track will take a curved course. Lastly, if the external opening is at a greater distance than an inch and a half from the anal margin, either anteriorly or posteriorly to the line, then the internal opening is always to be found in the middle line posteriorly opposite the interval between the sphincters, and the main track takes a curved course backwards (fig. 20, D,E.). The rule does not apply to the majority of fistulæ but only to certain types, which accounts for its not having received the recognition which it deserves. According to my own observations it is only applicable to the subsphincteric and the ischio-rectal types of fistulæ, representing rather less than 30% of the total number; but for these it is an accurate and valuable guide when an operation is being performed.

(3) *The main track* extends from the internal opening to the primary external opening, and may take a straight, curved or tortuous course. Its anatomical position in regard to the coats of the terminal portion of the rectum and of the tissues in its immediate vicinity determines the type of the fistula. The exact position of the main track of a fistula in regard to the muscular apparatus controlling the outlet of the rectum is of the utmost importance from the point of view of surgical treatment. Failure to recognize that all fistulæ are not of the same type is responsible for the disastrous consequences that sometimes result from operative treatment.

(4) *Offshoots or extensions from the main track.*—Whenever there is a free discharge of pus either from the internal opening or from the primary external opening, the formation of an offshoot from the main track is indicated. Repeated attacks of suppuration lead to the formation of multiple offshoots from the main track so that, in the course of time, a labyrinth of intercommunicating channels is formed. Some types of fistula are more prone to ramification than others. All fistulæ are at first unilateral, but secondary offshoots may extend across the middle line so that the fistula ultimately becomes bilaterally disposed. The offshoots from the main track are not necessarily confined to the same anatomical locality; thus, the secondary tracks in connection with an ischio-rectal fistula may be entirely located in the subcutaneous tissue, a complex fistula resulting to which the designation "fistula of the ischio-rectal type with *subcutaneous* extensions" should be applied. Again, an offshoot from an ischio-rectal fistula may be located in the submucous tissue, when an "ischio-rectal fistula" with *submucous* extension results. It is important, therefore, when operating upon different types of fistulæ, to bear in mind the possibility of offshoots existing in lymphatic areas other than that in which the main track is situated.

An offshoot from a unilaterally situated fistula when extending across the middle line to the opposite side, by reason of the fact that the lymphatics on both sides are symmetrically disposed, follows an exactly similar course as that taken by the main track of the original fistula, and is therefore a replica of it. The extension simulates the disposition of the original fistula, terminates in an external opening in a corresponding position to that occupied by the primary opening and gives rise to offshoots following a similar course to those taken by the offshoots from the original main track. The type of fistula which most commonly extends to the opposite side is the ischio-rectal, though the submucous type may occasionally do so.

GENERAL PRINCIPLES OF TREATMENT.

Whenever a fistulous communication with the interior of the anal canal or rectum has been established, spontaneous cure seldom results. The treatment, therefore, of an ano-rectal fistula is mainly operative, though in certain circumstances palliative measures may be adopted.

Palliative treatment.—This, though it may sometimes succeed in arresting progressing extension, rarely effects a permanent cure. It should, however, be always adopted in cases in which a patient's constitutional condition contra-indicates operative interference. Local treatment, such as the use of warm sitz baths and the application of fomentations to the perineum, is advisable. Daily evacuation of the bowels should be ensured by the use of mild aperients, but strong purgatives should be avoided, as violent peristalsis might force liquid fæces into the internal opening and set up active suppuration in the main track.

Operative treatment.—The surgical treatment of a fistulous track is comparable to the conversion of a subterranean tunnel into an open trench by digging away the earth, covering it from end to end, and then filling in the trench with new material until it is level with the surrounding surface. By adopting this principle the tissues overlying the main track of a fistula, from the primary external opening to the internal opening, are divided so that an open wound is created which is made to heal progressively from the bottom, and so efface the fistula. Offshoots extending into the surrounding tissues are dealt with in a similar manner. The principle underlying the surgical treatment of a fistula is to lay open the main track from end to end, together with all the offshoots extending from it. It is possible to efface all fistulæ in this way, but whether a satisfactory result is obtained or not depends upon the damage that may have been inflicted upon the muscular apparatus controlling the anal outlet. Although the majority of ano-rectal fistulæ communicate with the interior of the bowel by means of an internal opening, in only a small percentage of them is the muscular coat penetrated by the main track, but in these the laying open of the main track from end to end results in serious impairment of the muscular control of the anus. If all ano-rectal fistulæ were of the same type, the simple procedure of laying open the main track from end to end together with all offshoots from it would produce equally good results. Unfortunately, however, in some instances permanent loss of muscular control ensues. The explanation of this is that the anatomical relationship of the main track to the musculature of the anal outlet varies in different types of fistulæ. The position of the internal opening can usually be taken as an indication of the point where the main track passes through the bowel wall. The usual position of an internal opening is at the level of the interval between the internal and the external sphincter, which is approximately at Hilton's white line, but in some instances it may be found at a much higher level—for example, quite two or three inches above the anal margin. A high-lying internal opening does not, however, always indicate that the main track of the fistula penetrates the wall of the bowel at a corresponding level.

A great deal of controversy has centred round this point. Some authorities state that in their experience no harm results from laying open the main track of a fistula which has a high-lying internal opening, whereas others, of considerable experience, aver with equal conviction that in similar circumstances permanent loss of control inevitably results. When two such divergent opinions are expressed by those who have had considerable experience in the operative treatment of ano-rectal fistulæ it is obvious that there must be some explanation to account for the discrepancy. The truth is that neither group of observers has realized the fact that ano-rectal fistulæ differ widely in type, so that whereas both are right in the opinion expressed, both are also wrong.

Let us take, for example, the case of a submucous fistula having a high-lying internal opening such as represented in fig. 3. The main track of such a fistula is, throughout its course, superficial to the muscular coats of the bowel. Laying open the main track of such a fistula into the cavity of the bowel cannot possibly inflict any injury to the musculature and therefore no impairment of control can possibly result. Again, in the case of an ischio-rectal fistula with a submucous extension having an internal opening at the extremity of the submucous portion of the track, as shown in fig. 4, laying open the track from the external opening to the internal opening into the cavity of the rectum only inflicts injury to the external sphincter, from which it is common knowledge that impairment of control does not result. It is obvious, therefore, that those who hold the opinion that the laying open of a fistulous track, having a high-lying internal opening, may be carried out without inflicting impairment of control must have been fortunate enough to encounter fistulæ of the above types. On the other hand, those who have experienced the disastrous consequences of permanent loss of control have probably been unfortunate in encountering fistulæ of the type shown in fig. 5 (p. 86), during the early stages of their experience. It is apparent from a glance at that illustration that laying open the main track of that type of fistula (the para-rectal) into the cavity of the bowel would result in complete division of both sphincters, both muscular coats of the rectum as far as the site of the internal opening and, what is more important still, the point of fusion of the levator ani muscle with the external muscular coat of the rectum. The fibres of the levatores ani radiate from the periphery of the pelvis to the rectum, much in the same manner as do those of the ciliary muscle, towards the pupil. Contraction of the ciliary muscle dilates the pupil and contraction of the levatores ani expands the anal canal. When the margin of the pupil is divided, a V-shaped gap is produced by the unopposed contraction of the radiating fibres of the ciliary muscle. Exactly the same thing takes place when the point of fusion between the levator and the external muscular coat of the rectum is divided. A V-shaped gap is thereby produced owing to retraction of the edges of the wound and hopeless incontinence is the result.

Division of the internal sphincter is generally regarded as the cause of loss of control after fistula operations, but I have not found it to occur even after complete division of the muscle when laying open the main track of an intermuscular fistula. Other observers regard division of the external sphincter as the causative factor of impairment of control after operations for fistula, but these have evidently overlooked the fact that the external sphincter is generally completely divided during an operation for fissure without ill-effect. The position of the internal opening of a fistula is of very little consequence in determining the nature of the operation to be performed, but the anatomical situation of the main track in its relation to the musculature of the anal outlet is of the greatest importance.

An important principle involved in the operative treatment of a fistula is that the square area of the surface wound should be made at least twice as great as the square area of the rest of the wound. The most satisfactory way of increasing the surface area of a linear wound is to make incisions through the skin and subcutaneous tissue at right angles to the line of the main incision (fig. 6). I call these secondary incisions "relieving cuts." They should be made at points where there appears to be greatest tension along the margins of the main incision. No definite rules can be laid down in regard to their exact position or as to the number of incisions required, much depending upon individual experience as to the manner in which the wounds heal, but, provided that the surface area is increased to the requisite extent, the fewer the incisions required the better the ultimate result will be. Increase of the surface area of a wound may also be effected by removing healthy skin around the wound made by laying open the main track of the fistula and the offshoots from it. The objection to this procedure is that the wound takes longer to heal and the

deficiency of skin, resulting from extensive removal, is replaced by dense scar tissue which may interfere with the expansion of the anus during defæcation. When operating upon fistulæ lying at a great depth, such as those of the para-rectal type, the area of the whole wound may be so extensive that it is not possible to increase the area of the surface wound sufficiently, on account of lack of room. Under these circumstances the surface wound will have healed long before the remainder of the wound has been completely filled in. Nevertheless, the depth of the original wound will have been diminished considerably, in most instances by more than half of its original extent. In order to permit the remainder of the wound to be completely filled, the surface wound should be reopened to the requisite extent. When dealing with this type of fistula, the possibility of a second operation becoming necessary, in order to ensure complete effacement of the fistulous track, should never be lost sight of, and the patient should be warned of this beforehand.

General Principles in the Technique of an Operation upon a Typical Complete Fistula.

For an operation for fistula, the most suitable position of the patient is the lateral and semi-prone, on the side on which the primary external opening exists, except when the fistula is situated in the anterior part of the perineum, where the operation field is most conveniently exposed by the lithotomy posture. First of all, the exact position of the internal opening is determined by digital exploration of the anal canal, and then the course taken by the main track and the extent of the offshoots from it are carefully mapped out by grasping the peri-rectal tissues between the index finger inside the rectum and the thumb upon the skin surface of the ischio-rectal fossa. The point of a probe-director is then introduced into the main track through the primary external opening. It sometimes happens that the orifice is so contracted that difficulty is experienced in inserting even the smallest probe into it. In these circumstances the orifice should be enlarged by a small incision at right angles to the line of the main track. As soon as the probe-director has fairly entered the main track, it should be gently passed along it in a direction towards the internal opening. No force should be used, lest a false passage be made. When the main track takes a straight course no difficulty is experienced in introducing the probe as far as the internal opening, where the point can readily be made to protrude through it. In those cases, however, in which the main track takes a curved course (fig. 25, p. 90), some difficulty may be encountered in reaching the internal opening, on account of the inability of the probe to adapt itself to the curves of the track. Accordingly, in order to avoid making a false passage, the point of the probe should be forced through the skin at the spot where its further progress has been arrested. The tissues overlying the probe are then divided, thus exposing a portion of the track. The probe is then re-introduced into the track and passed along it until its point protrudes through the internal opening. Should the passage of the probe be again impeded by a curve in the track, the manœuvre above described must be repeated. As soon as the probe-director has entered the anal canal, its point should be hooked down by the index finger and brought out through the anus. The overlying tissues, including the external sphincter muscle in all cases in which the track passes beneath that muscle, are then divided completely so as to liberate the probe. The floor of the main track has thus been exposed to view in its entirety and can be readily recognized by the granulation tissue lining it. A careful search is then made along the floor and sides of the exposed track for apertures leading into offshoots. When such an offshoot is found the probe should be passed along it to its extremity and forced through the skin at that point, should it terminate in a cul-de-sac. When all existing offshoots have been laid open, relieving cuts, in order to increase the surface area of the wound to the required extent, should be made at points where they are considered to be necessary. Finally, all overhanging or undermined edges of skin should be removed and the entire wound carefully packed with strips of gauze and cotton-wool.

General Principles of After-Treatment.

The after-treatment of a fistula wound is exceedingly important. A perfectly successful operation may fail to effect a cure if the details of after-treatment are not attended to. The primary object to be obtained is that the wound resulting from the operation should heal progressively from its deepest part throughout its entire extent. When the wound is superficial there is no difficulty, and the healing process proceeds without interruption until the granulation tissue becomes level with the surrounding skin and the surface is completely covered by epithelium. In those cases, however, in which the main track lies at a considerable depth and pursues a curved course, the surfaces of the more superficial parts of the wound are apt to come into contact with one another and adhere, unless kept apart. In this way the deepest part of the wound may escape obliteration, and the main track of the fistula is re-established by the process known as "bridging." In order to prevent bridging the surfaces of the deeper portions of the wound should be kept apart by interposing a thin layer of cotton-wool or a strip of gauze between them. On no account should the wound be tightly packed. The only occasion when a fistula should be tightly packed is just after the operation has been completed—never afterwards. Tight packing not only impedes the healing process but prevents the formation of granulation tissue, with the result that the wound ultimately heals with a depressed scar, which, especially when it traverses the anal orifice, is one of the commonest causes of impaired control after operations for fistula.

A fistula wound which is healing healthily is practically free from suppuration. Whenever pus wells up in the wound it is an indication that one of three conditions is present: (1) Bridging has occurred at some part of wound; (2) an offshoot has escaped detection during the operation; or (3) an offshoot, which did not exist at the time of the operation, has developed subsequently as a consequence of infected tissue having broken down. Whenever, therefore, an excess of pus is found to exist, the wound should be carefully explored with a probe, in order that the exciting cause of the suppuration may be ascertained and dealt with by a secondary operation without delay.

The Subcutaneous Type of Ano-Rectal Fistula.

The subcutaneous fistula is entirely confined to the subcutaneous tissue in the immediate vicinity of the anus, both the main track and any existing offshoots from it being usually superficial to the deep fascia and to the external sphincter muscle. The abscess preceding its formation is generally due to suppuration occurring in a localized hæmatoma occasioned by the rupture of a dilated circumanal vein (sometimes called a thrombotic pile), a suppurating circumanal sebaceous follicle or to septic thrombosis or lymphangitis originating in a fissure. The resulting fistula is never extensive, is invariably unilateral, and presents three varieties:—

(*a*) *The blind external subcutaneous fistula* is nearly always due to a suppurating circumanal hæmatoma, though occasionally it may be of tuberculous origin. The external opening is usually small and is often difficult to find when situated in a sulcus between adjacent anal rugæ. The main track, often not more than half an inch in length, is directed towards the anal margin and is entirely superficial to the external sphincter muscle. This variety may exist at any part of the anal circumference.

(*b*) *The blind internal subcutaneous fistula* (fig. 7, p. 86) is invariably associated with a fissure, and is due to septic lymphangitis. The internal opening is situated at the lower edge of the fissure and can usually be displayed when the anal margin is everted. The main track radiates in a straight line from the fissure and is generally situated close to the middle line and nearly always on the right side of it. There are no offshoots from the main track.

(*c*) *The complete subcutaneous fistula* (fig. 8, C, D, p. 86) is a later stage of the preceding variety. The external opening is usually situated about one inch from the anal margin. The internal opening is situated at the lower margin of the fissure and is generally larger than in the blind internal variety. On this account fæcal matter is apt to pass into the track when the bowels act, and set up active suppuration. Repetition of the inflammatory process may lead to the formation of an offshoot which is invariably single and extends beyond the primary opening in the same radial line as that taken by the main track. A secondary opening may then appear at the extremity of the offshoot. Whenever active suppuration occurs in the main track of a subcutaneous fistula arising from a fissure, a submucous fistula may be associated with it (fig. 8, A, B). This possibility should never be lost sight of, because if the existence of the submucous fistula is overlooked, complete effacement of the subcutaneous fistula will not cure the patient of his symptoms.

Differential diagnosis.—Since the main track of a subcutaneous fistula is entirely confined to the subcutaneous tissue, the induration caused by its presence is superficial and can be readily picked up between the index finger and thumb and lifted, as it were, away from the underlying structures. In those instances in which the fistula has existed for a considerable length of time, perhaps for several years, there is marked thickening of the wall of the fistula, the result of thwarted efforts at repair, and therefore the course taken by the main track can be clearly defined by surface palpation. When the finger is introduced into the rectum and the tissues of the ischio-rectal fossa are grasped between it and the thumb externally, induration in the ischio-rectal fossa is found to be absent, thus serving to distinguish the subcutaneous type of fistula from the ischio-rectal, which often possesses subcutaneous extensions in connection with its main track. When deep-seated induration is detected, an ischio-rectal fistula with subcutaneous extension exists. As the external opening of a subcutaneous fistula is often situated close to the anal verge, it may be confused with that of a submucous fistula. The point is readily settled by introducing a probe into the external opening. Should the probe pass deeply into the main track without resistance, there can be no doubt that the opening leads into the track of a submucous fistula.

Clinical course.—When once established, the subcutaneous fistula continues to discharge pus from the external opening. When caused by a fissure, pain after defæcation, persisting for several hours afterwards, is a prominent symptom. If the internal opening is large, fæcal matter is apt to enter the main track and set up active inflammation occasioning attacks of pain in the fistula itself. In these circumstances secondary abscesses are formed, with the attendant symptoms of pain, local tenderness, and pyrexia. Occasionally, when the main tract is short, the whole of it may become epithelialized and spontaneously cured.

Operative technique.—The subcutaneous fistula is the simplest form of fistula, consisting, in most cases, of an external opening and an internal opening connected by a straight, superficially situated track. The operation necessary to effect a cure is therefore of the simplest kind. A probe-pointed director is introduced into the external opening, made to protrude through the internal opening, and then liberated by dividing the tissues over it. The result is a linear incision of shallow depth. With the exception of the corrugator cutis ani, no muscular structures are divided and, consequently, the wound heals without the slightest risk of impairment of control. As the edges of a linear incision are apt to turn in during the healing process, the resulting scar may become depressed and groove-like. In order to prevent this and to expedite healing, a short relieving cut should be made on either side of the primary incision. When a fissure co-exists the pecten band should be divided in the right posterior quadrant of the anal orifice.

The pecten band is a fibrous ring due to the deposit of fibrous tissue in the submucosa of that portion of the anal canal which Stroud described as the pecten.

This area is bounded above by the free borders of the valves of Morgagni (spoken of as the pectinate line) and below by Hilton's white line. Whenever an operation is being performed for a subcutaneous fistula caused by a fissure, a careful search should always be made for a submucous track extending upwards from the upper edge of the fissure. When such a submucous track exists, its presence can readily be detected by exploring the upper part of the fissure with a probe. The submucous track should then be dealt with according to the method advised for submucous fistula (p. 73).

After-treatment.—Since the wound resulting from laying open the main track of a subcutaneous fistula and the offshoots from it, is shallow, the packing introduced into it at the time of the operation usually comes away when the dressing is changed twenty-four hours afterwards. In those cases in which the pecten band has been divided, the small pledget of cotton-wool, which was inserted between the edges of the pectenotomy wound, should not be disturbed until the bowels are opened on the fourth day after the operation. The surface of the wound should be irrigated twice daily with an antiseptic solution. At the expiration of a week or ten days the surface of the wound is usually covered throughout by healthy granulations, and healing should be complete at the end of three weeks. In those cases in which a submucous track has been treated by the ligature method (fig. 11, p. 87) the ligatures, together with the slough, become detached on the eighth or ninth day and are voided in the stools. On the twelfth day, and every day afterwards until the wounds have healed, the finger should be passed into the anal canal to ensure healing taking place progressively from the bottom of the wound.

The Submucous Type of Ano-Rectal Fistula.

The submucous fistula is confined to the submucosa of the anal canal and lower portion of the rectum, and is usually limited to one side of the bowel, though occasionally it may extend to both sides. It originates as an abscess in the submucosa of the rectal ampulla, and is due either to septic phlebitis or lymphangitis or to septic infection of blood-clot which has been extravasated beneath the mucosa as the result of the puncture of a hæmorrhoidal vein by a foreign body, or to rupture of a vein during a violent straining effort. Occasionally the abscess is of tuberculous origin. Owing to the loose texture of the submucous tissue, the abscess extends laterally as well as downwards towards the anus, where it discharges its contents through an opening either at the anal margin itself or through the skin within half an inch of that point.

This type of fistula presents four varieties: (*a*) Blind external submucous; (*b*) blind internal submucous; (*c*) complete submucous; (*d*) bilateral submucous.

(*a*) *The blind external submucous fistula* (fig. 9, p. 86) is generally the result of a submucous hæmatoma. The extravasated blood soon becomes infected and suppurates freely. The resulting abscess gravitates towards the anus, and in doing so takes an oblique course downwards and backwards until it reaches the anal margin where it finds an exit through the skin. The external opening is usually to be found either in the right or in the left posterior quadrant, and is generally situated within half an inch of the anal verge. The main track extends obliquely upwards and forwards and terminates in a cul-de-sac (fig. 9, A). As a rule, the track is situated close to the muscular coat of the bowel beneath the hæmorrhoidal vessels.

(*b*) *The blind internal submucous fistula* (fig. 6, A, p. 86) is the result of a submucous abscess which has been caused by septic phlebitis or lymphangitis. The septic process usually starts in a lesion situated in the anal canal such as a fissure, a torn-down anal valve, laceration of the mucosa of the anal canal during the passage of a foreign body, e.g., a fish-bone, ulceration of the interior of a valve of Morgagni or a puncture by the needle of a syringe used for the injection treatment of internal hæmorrhoids. The internal opening is situated in the anal canal at the site of the

initial lesion and affords a ready vent for the pus in the abscess cavity, so that the abscess seldom attains large dimensions. Consequently the main track is seldom more than an inch long and generally takes a course parallel to the longitudinal axis of the rectum.

(*c*) *The complete submucous fistula* (fig. 3, p. 86) is the least common of the varieties of submucous fistula. It is invariably the result of an abrasion of the surface of the rectal mucosa above the level of the levatores ani. The abrasion may be due to puncture or laceration by a foreign body (fragment of bone) or to the partial tearing through of the pedicle of a fibrous or an adenomatous polypus.

An extensive abscess is formed as the result of acute septic infection, and although the pus escapes freely through an internal opening situated at the site of the original lesion, it also tracks down towards the anus and discharges through an opening situated within half an inch of the anal margin.

(*d*) *The bilateral submucous fistula* (fig. 10, p. 87) is always the result of a submucous abscess situated on the posterior wall of the rectum above the level of the levatores ani. Owing to the spasmodic action of the levatores, induced by the presence of the abscess, the anal canal is firmly compressed and the purulent collection, unable to track downwards on that account, extends transversely beneath the mucosa on both sides above the level of the levatores. Eventually, the pus tracks down towards the anus exactly in the middle line posteriorly and discharges itself through an opening situated at the level of Hilton's white line (fig. 10, C). As soon as the pus has been evacuated the abscess cavity contracts, but the lateral portions of it remain as bilateral tubular extensions from the upper extremity of the median main track (fig. 10, A, B). These lateral extensions usually terminate in a cul-de-sac and are generally situated beneath the hæmorrhoidal veins (fig. 10, D). The T-shaped disposition of the submucous induration caused by the track of the fistula is characteristic of the bilateral submucous fistula.

Differential diagnosis.—It is of the utmost importance, from the point of view of surgical treatment, that a fistula of the submucous type be distinguished from one whose main track is situated externally to the muscular coat of the rectum, as in the case of the para-rectal fistula. In the complete variety of either type there is an external opening situated in the peri-anal region, associated with a high-lying internal opening through which the point of a probe-director can be made to protrude (figs. 3 and 5).

Laying open the track of a fistula of the submucous type is not followed by the slightest degree of impairment of the power of control, but if a similar procedure be carried out in a fistula of the para-rectal type permanent incontinence will ensue. In order to distinguish between the two types, a probe-director should be introduced into the main track through the external opening and pushed onwards until its point protrudes through the internal opening. If the edges of the groove in the director can be felt by the examining finger, the track is situated in the submucosa, but if they cannot be felt, then the track is outside the wall of the rectum (fig. 16, I, p. 88).

Clinical course.—The submucous fistula differs from all other types by not exhibiting any tendency to extend by means of the development of secondary offshoots from the main track. So soon as the contents of the original abscess have been evacuated, the abscess cavity gradually contracts into a linear track. As the opening through which the pus has been evacuated is situated at the most dependent part of the track, there is effective drainage. When there is an external opening the escape of pus is generally continuous, but in cases in which the opening is situated in the anal canal, the discharge is intermittent, taking place either during an action of the bowels or when flatus is being voided.

Operative technique.—The principle of laying open the main track of a fistula throughout its full extent can be safely applied to fistulæ of the submucous type, provided that the incision is made towards the lumen of the bowel and not in the

opposite direction. The tissues thus divided consist only of mucous membrane and the blood-vessels contained in the submucous tissue when the track lies beneath them, so that there is no danger of damaging the muscular control of the anal outlet. Cutting across the hæmorrhoidal arteries and veins causes free bleeding which may be exceedingly difficult to control, especially when the track of the fistula extends upwards for two or three inches above the anal verge. When the track lies between the branches of the hæmorrhoidal vessels or is superficial to them, there is no danger, but, since the track passes beneath the vessels obliquely in the majority of instances, it is impossible to lay it open without also dividing them. The method of laying open the track with the knife is unsuitable for this type of fistula and therefore the ligature method should always be employed. When an external opening is present, the portion of the track between it and Hilton's white line can be safely incised, as bleeding points in that situation can readily be controlled, but the remainder of the track should be treated in the following manner: A probe-director is introduced into the lower extremity of the track and passed along until the upper end of the track has been reached. If an internal opening exists at that point, the point of the probe is pushed through it, but, if not, the probe must be forced through the mucosa. Since submucous tracks usually take an oblique course upwards, the point where the probe emerges through the mucous membrane is seldom more than two inches above the level of the anal margin, so that the end of the probe can readily be hooked down by the finger and made to protrude through the anus without lacerating the mucosa. Two stout silk ligatures (No. 16 plaited) are then attached to the end of the probe and drawn through the track (fig. 11, A, p. 87). Without interlocking the ligatures, one of them is tied tightly and then the other is tied a little to one side of it so as to include the portion of the mucosa forming the superficial wall of the track (fig. 11, B). The mucosa included between the ligatures necroses, and when the slough separates, the track is found to have been laid open from end to end just as effectively and with more safety to the patient than when the method of incision has been employed.

Those who follow blindly the doctrine that a fistulous track having a high-lying internal opening should never be laid open into the bowel, divide the tissues surrounding the track in the opposite direction, that is to say, outwards and away from the lumen of the bowel. The effect is exactly the same as when the track of a para-rectal fistula is laid open into the lumen of the rectum. I have seen several instances of permanent incontinence result from this plan of operating upon a submucous fistula. There is no doubt, therefore, that those who practise it fail to recognize the important fact that fistulæ possessing a high-lying internal opening may differ in regard to the anatomical relationship of the main track to the musculature of the anal outlet, upon the preservation of which the power of control so much depends.

After-treatment.—The bowels should be confined for four days and then opened by a brisk purgative. Twenty-four hours before the purgative is administered, four ounces of olive oil should be introduced through the anus and retained. An ounce of liquid paraffin is given each succeeding night, combined with a mild purgative, to ensure a daily movement of the bowels. The application of a ligature to the mucous membrane of the rectum does not cause pain, so that sedatives are seldom necessary. The ligatures, together with the slough, usually separate on the eighth or ninth day and are voided in the stools. On the twelfth day the index finger should be passed into the rectum to ascertain, primarily, whether the ligatures have separated, and secondly, to find out whether any part of the track remains unopened. On each succeeding day, until healing is complete, the finger should be passed into the rectum to ensure that the margins of the exposed track do not become approximated and re-establish the fistula. Epithelialization of the granulating surface is usually completed in nineteen days in men and in sixteen days in women.

The Intermuscular Type of Ano-Rectal Fistula.

The intermuscular ano-rectal fistula is one in which the main track is situated between the internal sphincter and the longitudinal muscular coat of the rectum (fig. 12, p. 87). It is the rarest type and is seldom more than an inch in length. It is due to septic lymphangitis following suppuration in a sinus of Morgagni and is generally associated with a fistula of the subsphincteric type, but sometimes is found to exist by itself. The main track takes a straight course parallel to the longitudinal axis of the bowel, does not give rise to offshoots, and terminates in a cul-de-sac. There is an excellent example in the museum of St. George's Hospital, the dissected specimen displaying the track beneath the fibres of the internal sphincter. There is only one variety of this type, namely, the blind internal, the internal opening being situated at the entrance to a sinus of Morgagni about a quarter of an inch above Hilton's white line.

Differential diagnosis.—The intermuscular fistula must be distinguished from one of the submucous type, and especially from the submucous extension from either the subsphincteric or the ischio-rectal types. The main track of the intermuscular fistula is always perfectly straight and seldom exceeds an inch in length. When a probe-director is introduced into the track, the probe cannot be distinctly felt. The track of the submucous fistula, or of a submucous extension from an ischio-rectal or from a subsphincteric fistula, is seldom straight, usually takes an oblique course forwards and upwards, and generally terminates in a cul-de-sac which can be distinctly felt as a rounded enlargement of a linear induration. When a probe-director has been introduced along such a submucous track, the margins of its groove can be easily recognized by the examining finger.

Clinical course.—When established, the track never becomes spontaneously obliterated, owing to the constant action of the internal sphincter muscle. Pus is formed continuously and escapes whenever the bowels act. In those instances in which an intermuscular track co-exists with either a subsphincteric or an ischio-rectal fistula and has escaped detection during an operation, the wound fails to heal completely, a slight discharge of pus persisting indefinitely, unless its presence is discovered.

Operative technique.—Since the main track of the fistula seldom exceeds an inch in length, there need be no hesitation in laying it open from end to end into the lumen of the bowel because, even if there is free bleeding as the result of cutting through the hæmorrhoidal vessels, the bleeding points are within easy reach and can readily be controlled. A probe-director should therefore be inserted into the track through the internal opening, and after traversing the whole length of the track, its point should be forced through the wall of the bowel into its lumen. The tissues covering the probe, which of course include the internal sphincter, are then divided completely. I have had occasion to divide the internal sphincter in this way on several occasions and have never observed the slightest impairment of control to result in consequence.

After-treatment.—This is practically the same as that described for a submucous fistula, and should be conducted upon those lines whenever an intermuscular fistula exists by itself. In those cases in which either an ischio-rectal or a subsphincteric fistula co-exists, the treatment applicable to those conditions should also be carried out.

The Para-Rectal Type of Ano-Rectal Fistula.

The para-rectal fistula is the result of an abscess which has formed in the para-rectal space, bounded internally by the external coat of the rectum and externally by the fascia propria. The compartment so formed contains the *lymphatic sinus of the rectum* and the peri-rectal fatty tissue. The efferent lymph channels emanating from the intramural lymphatic system of the rectum empty themselves

directly into the lymphatic sinus, so that septic lymphangitis originating in the rectum may terminate in para-rectal suppuration. An abscess in the para-rectal space is shut off by the dense fascia propria from the stratum of loose cellular tissue existing between the pelvic peritoneum and the levatores ani, constituting the superior pelvi-rectal space of Richet (fig. 2, p. 85). The para-rectal abscess is situated in the space between the fascia propria and the rectum, and is always due to a lesion in the rectum from which septic phlebitis or lymphangitis extends.

In some instances the septic process is due to puncture of the wall of the rectum above the level of the levatores, by a foreign body, such as a fish-bone. Whether it is the result of septic thrombosis of the veins passing through the wall of the rectum, or to septic lymphangitis or to perforation of the rectal wall by a foreign body, the abscess cavity communicates with the interior of the bowel by means of a high-lying internal opening (fig. 13, A, p. 87). An abscess thus situated, being unable to invade the superior pelvi-rectal space on account of the attachment of the fascia propria to the recto-vesical fascia, may extend completely round the rectum. The pus may then invade the subjacent ischio-rectal fossa on the same side by passing through the interval between the levator and the coccygeus, or between the fasciculi of the levator itself (fig. 14, B, p. 88). Finally, it escapes through an opening on the skin surface and in some instances by an internal opening situated in the middle line posteriorly, at the level of the interval between the internal and the external sphincters (fig. 15, B, p. 88). In rare instances the collection of pus above the levator finds its way downwards in the middle line posteriorly between the coccygei and invades both ischio-rectal fossæ simultaneously, eventually discharging through symmetrically placed external openings (fig. 16, C, D, p. 88).

There are three varieties of the para-rectal fistula, namely: (*a*) blind internal para-rectal; (*b*) complete para-rectal; (*c*) bilateral para-rectal.

(*a*) *The blind internal para-rectal fistula* (fig. 13) is in reality the primary stage in the development of the complete variety, which is the form in which the para-rectal fistula is most commonly met with. Its onset is characterized by acute constitutional disturbance associated with pain deeply seated in the pelvis. The pain may be very acute and may radiate to the lumbar and sacral regions and, in some instances, extend down the back of the thighs along the course of the great sciatic nerve. Unless symptoms definitely referable to the rectum develop, the presence of a para-rectal fistula in its early stage may easily be overlooked. So soon as the pus has invaded the ischio-rectal fossa, a tender swelling, associated with redness of the skin in the neighbourhood of the anus, points to the supervention of an ischio-rectal abscess. A copious discharge of pus from the rectum is significant of the existence of a deep-seated blind internal fistula, so that an early opportunity should be taken of examining the rectum with the proctoscope. When a blind internal para-rectal fistula exists, a copious discharge of pus will be seen to be taking place from a single point in the rectal wall, above the level of the levator ani. When the finger is introduced into the rectum a definite tense elastic swelling is felt encroaching upon the lumen of the bowel and generally extending upwards beyond the reach of the finger. Should the lower margin of the swelling be situated above the level of the levator ani, it is evidence that the pus has not yet made its way into the ischio-rectal fossa (fig. 13).

(*b*) *The complete para-rectal fistula* is a later stage of the preceding variety. With the formation of an external opening a copious discharge of pus takes place and all previous symptoms of an acute ischio-rectal abscess rapidly disappear. If the patient is now seen for the first time, the external appearances are those of an ischio-rectal fistula, the external opening being situated at least an inch and a half distant from the anal verge and a trifle in front of the transverse anal line or slightly posteriorly to it. The main track, however, passes deeply in a direction parallel to the longitudinal axis of the rectum, so that a probe introduced into the external

opening easily enters the track to a depth of three or four inches. If the finger is then introduced into the rectum, the point of the probe will be felt to protrude into the cavity of the bowel through an internal opening situated above the level of the levator ani. Throughout its course the main track is situated outside the wall of the rectum, and as it passes through the levator ani or between that muscle and the coccygeus it is also external to the point of fusion of those muscles with the longitudinal muscular coat of the rectum (fig. 15, p. 88).

(*c*) *The bilateral para-rectal fistula* is the most extensive and also the most complex of the ano-rectal fistulæ. The original abscess, having completely encircled the rectum, extends downwards through the interval between the coccygeus muscles, in the middle line posteriorly, and gives rise to septic lymphangitis in both ischio-rectal fossæ, with the result that an ischio-rectal abscess develops on both sides. Since the disposition of the lymphatics is symmetrical on both sides, when the collections of pus in the ischio-rectal fossæ find an exit on the skin surface, the resulting primary external openings are usually symmetrically placed (fig. 16, C, D, p. 88). Should offshoots subsequently develop, the secondary external openings in connection with them are not necessarily symmetrical, as the tendency is for the greater number to develop on the right side. As the result of the invasion of the ischio-rectal fossæ, and also as a consequence of septic lymphangitis, an internal opening usually develops in the middle line posteriorly between the internal and the external sphincters (fig. 16 B). This is a secondary internal opening and must not be mistaken for the primary internal opening which is situated much higher up and always above the level of the levator ani (fig. 16 A.) In addition to the bilateral extensions from the main track above the levatores and those situated in the ischio-rectal fossæ, there may also exist submucous extensions from the internal openings, unilaterally or bilaterally disposed, so that the bilateral variety of the para-rectal type of ano-rectal fistula may combine several of the types in one complex fistula.

Differential diagnosis.—In the early stage, when still confined in the space above the pelvic diaphragm, the blind internal para-rectal fistula may be mistaken for a high-lying submucous abscess. Both produce a globular swelling encroaching upon the lumen of the bowel. Since the swelling produced by the para-rectal fistula is outside the wall of the bowel, the mucosa is freely movable over it; whereas it is smooth and immobile in the case of the submucous abscess. When the para-rectal fistula has extended into the ischio-rectal fossa, the features of an ischio-rectal abscess are simulated, but the fact that the swelling in the ischio-rectal fossa extends upwards beyond the level of the levator points to its true nature.

When there is an external opening into which a probe passes deeply, the para-rectal fistula may be mistaken for: (1) a submucous fistula; (2) a pelvi-rectal fistula; and (3) a pre-sacral fistula.

The position of the external opening serves as a useful guide. The external opening of a submucous fistula is usually situated within half an inch of the anal verge. That of a pelvi-rectal fistula is found to be at least an inch and a half from the anal verge and slightly posterior to the transverse anal line. That of the retro-rectal (pre-sacral) is generally located at the level of the tip of the coccyx and about one inch distant from it, whereas the external opening of the para-rectal fistula is generally found at a greater distance than an inch and a half from the anal verge and slightly in front of the transverse anal line. Moreover, neither the pelvi-rectal nor the retro-rectal fistula possesses an internal opening.

Clinical course.—The development of an abscess in the para-rectal space produces the symptoms of pelvic cellulitis. Until symptoms definitely referable to the rectum develop, an abscess in the para-rectal space may easily be overlooked and, therefore, digital exploration of the rectum should never be omitted. Sooner or later the ischio-rectal fossa becomes invaded and then the implication of the rectum is

apparent. Eventually, unless the ischio-rectal abscess is freely incised, there develops a primary external opening through which the pus is evacuated. Offshoots from the main track in the ischio-rectal fossa may subsequently develop, with the result that numerous secondary external openings appear. As a rule, when offshoots from the main track are present, an internal opening, situated in the middle line posteriorly between the external and the internal sphincters, also exists (figs. 15, B, and 16, B, p. 88).

Operative technique.—The principle of laying open the main track of an ano-rectal fistula into the bowel throughout its extent from the external opening to the internal opening must never be applied to a para-rectal fistula. A glance at figs. 5 and 15 show that by doing so not only would both the external and the internal sphincters be divided, but the point of fusion of the levator ani with the longitudinal coat of the rectum, together with the whole thickness of the bowel wall as far at the high-lying internal opening, would be divided as well, resulting in permanent and irremediable incontinence. The tissues on the outer aspect of the main track alone should be divided as far as but not beyond the point where the main track passes through the wall of the rectum (fig. 18, p. 88). The incision through the levator ani is made in the direction of its fibres and not transversely. The surface wound should be extensive, as shown in fig. 18 by the line B—C, so that the area of the surface wound will be greater than the combined area of the remainder of the wound. Since the details of technique vary in some particulars when operating upon para-rectal fistulæ in the four stages represented by figs. 13, 14, 15, and 16, it will be as well if they are described separately.

(1) *In the early stage of the blind internal para-rectal fistula.*—When the finger is introduced into the rectum, a globular swelling is felt above the level of the levator ani (fig. 13, p. 87). With the finger acting as a guide within the rectum, the point of a long straight bistoury is introduced through the skin at the point A in (fig. 17, p. 88). The blade of the knife is passed onwards, outside the wall of the rectum, parallel to the finger, until the cavity of the abscess has been penetrated, as indicated by the escape of pus along the knife. When introducing the knife the greatest care must be exercised in order to avoid penetrating the wall of the rectum. So soon as the abscess cavity has been penetrated, the knife should be withdrawn in such a way that the tissues are divided away from the rectum, as indicated by the line A— B in fig. 17. This incision is then extended by making another incision C—D at right angles to its inner extremity. The resulting wound is pyramidal in shape and, provided that the surface incisions have been made sufficiently long, the square area of the surface wound will be greater than the combined area of the remainder of the wound. The finger should then be introduced into the abscess cavity in order to ascertain whether a foreign body, such as a fish-bone, is present. I have found pins, needles, and fish-bones in the cavities of this type of fistula on several occasions.

(2) *When a blind internal para-rectal fistula has extended to the ischio-rectal fossa* (fig. 14, p. 88).—Owing to the fact that the abscess has extended into the ischio-rectal fossa, the pus is nearer the surface and the operation is much less difficult, because there is no danger of the rectum being penetrated during the introduction of the bistoury. The abscess cavity in the ischio-rectal fossa is laid open freely by incisions similar to those employed in the operation for the preceding stage. The aperture in the levator ani leading into the para-rectal space is sought for and enlarged in the direction of its muscular fibres. The cavity above the levator is then explored with the finger, in order to ascertain its dimensions and also to disclose the presence of a foreign body, should one exist. Should it be found that the abscess cavity extends upon the upper surface of the levator for a considerable distance, on either side of the aperture through the muscle, a short transverse cut through the fibres of the levator should be made on both sides of the radiating incision, but these must be as limited as possible commensurate with providing adequate drainage.

(3) *When a blind internal para-rectal fistula has become complete* (fig. 15).—A probe-director is introduced into the primary external opening and gently passed along the track in the ischio-rectal fossa as far as it will travel without force. The point of the probe is then pushed through the skin if a secondary external opening does not exist. The tissues overlying the probe are then divided to expose the track in the ischio-rectal fossa. A careful search is then made for offshoots from the track and if any are found they should be laid open freely. When this has been done the aperture through the levator ani is sought for and dealt with as described above. When an internal opening is found to exist in the middle line posteriorly between the sphincters, the portion of the track extending beneath the external sphincter to the internal opening should not be laid open until the deep part of the main track has been obliterated by the healing process. If the portion of the track extending beneath the external sphincter is laid open at the time of the main operation, fæces are apt to enter the deep part of the wound during an action of the bowels, and may greatly impede the process of repair. Nevertheless, the wound will not heal completely until this portion of the track has been laid open, so that in these cases an operation in two stages is necessary.

When the para-rectal fistula is bilateral.—The tracks in both ischio-rectal fossæ are laid open completely, commencing on the side on which the primary external opening appeared. The track leading into the portion of the fistula situated above the levatores is found to be situated in the middle line posteriorly, between the coccygeus muscles. The muscles are divided for a short distance on either side, in order to drain the lateral extensions of the cavity above them (fig. 16, E, F). The surface wounds are extended by relieving cuts (fig. 6) wherever required. The portion of the track passing beneath the external sphincter to the internal opening, which is situated between the sphincters in the middle line posteriorly, should not be laid open until the deep parts of the wound on both sides have been filled in.

In all operations undertaken for a para-rectal fistula the high-lying internal (primary) opening should not be interfered with. It will close completely as soon as the deep portion of the wound has been obliterated by the healing process.

After-treatment.—However carefully and accurately an operation for a para-rectal fistula may have been carried out, unless the after-treatment is conducted with scrupulous care and attention to detail, the operation may fail to effect a cure. This is due to the difficulty in securing adequate drainage for the portion of the main track which lies above the level of the levator ani, without inflicting serious damage to the muscle. Should the incision made through the levator close before the cavity above it has been obliterated, a sinus will remain which will continue to discharge pus indefinitely and prevent complete closure of the surface wound. Especial care, therefore, should be devoted to the part of the track above the levator during the early stages of the after-treatment. The gauze packing introduced into the cavity of the wound after the operation had been completed, should be left in situ for at least four days and then removed. The advantage of leaving the packing in the wound for that length of time is that, after its removal, the sides of the cavity do not fall together as readily as they otherwise would. After the original packing has been removed, the wound must on no account be repacked.

One of the chief reasons why fistulous tracks fail to close after an operation is because they are repacked persistently. It stands to reason that, if a cavity is packed continuously, it is a physical impossibility for healing to take place. The packing prevents the growth of granulation tissue and delays the process of repair. If there is a tendency for the surfaces of the wound to fall together, they should be kept apart by interposing a thin layer of wool between them, to prevent them from adhering together before the deep part of the wound has closed in.

Careful irrigation of the entire wound cavity, at least twice daily and also after each action of the bowels, is all that is necessary to ensure steady healing taking

place from the bottom of the wound. For this purpose there is nothing more efficacious than a strong solution (1 in 500) of perchloride of mercury. When, after the expiration of ten days, the surface of the wound is covered by healthy granulation tissue, the perchloride is dispensed with and a solution of iodine (2 dr. to a pint) is substituted for it. In cases of long standing, the growth of granulation tissue is usually slow. This is due to excessive induration of the tissues surrounding the track, and it becomes necessary to destroy the indurated tissue in order to expedite the growth of the granulations. For this purpose there is nothing better than nitrate of silver. When the track is straight it can be easily applied to the whole surface by means of the solid stick, but if the track is tortuous, or if there are offshoots extending from it, a saturated solution (960 gr. to the ounce) should be injected into the track by means of a suitable syringe. As the result of the application of nitrate of silver the indurated wall of the track sloughs and, when the slough exfoliates, at the expiration of six days, a healthy granulating surface is left which proceeds to obliterate the cavity with normal rapidity. The closing of the wound, resulting from the operation upon a para-rectal fistula, may take from two to six months according to its depth and its duration. Should the surface wound close before the deep part has completely filled in, a secondary operation is necessary to reopen the surface wound to the required extent.

The Subsphincteric Type of Ano-rectal Fistula.

The subsphincteric fistula, as its name implies, is situated beneath the external sphincter muscle (fig. 19, p. 89). It is prevented from extending into the fatty tissue of the ischio-rectal fossa by the fascial expansion, by means of which the longitudinal muscular coat of the rectum is inserted into the skin at the outer border of the external sphincter muscle. It will be remembered that the longitudinal muscular fibres of the rectum, after blending with the levator ani, terminate in a fascial expansion which divides into two strata, an outer and an inner. The outer stratum passes on the deep aspect of the external sphincter to be inserted into the skin at the outer border of that muscle; this stratum forms a compartment for the external sphincter and intervenes between it and the ischio-rectal fat. The inner layer passes through the external sphincter, dividing it into a superficial and a deep portion, and is also inserted into the skin at the outer border of the muscle. The efferent lymphatics from the anal canal, on their way to join the subcutaneous lymphatic plexus at the outer border of the external sphincter muscle, pass beneath the muscle, between it and the stratum of the fascial expansion which separates it from the ischio-rectal fat. Some of the lymphatics also pass between the superficial and the deep portions of the external sphincter muscle. Venous trunks from the anal canal also follow a similar route in order to join the circumanal veins. As the result of septic phlebitis, or lymphangitis, an abscess may form either between the external sphincter and the fascia, or between the superficial and the deep portions of that muscle. Such abscesses find an exit at the outer border of the muscle, the primary external opening of the resulting fistula being situated at a point between an inch and an inch and a half distant from the anal verge (fig. 19). The initial lesion is usually an ulcer in one of the sinuses of Morgagni, laceration at the base of the pedicle of a small fibrous polypus, or a fissure in the middle line, posteriorly, of the anal margin. Occasionally the septic focus is the result of puncture or laceration of the mucosa of the anal canal during the passage through the anus of a fish-bone or fragment of bone which has been swallowed.

The subsphincteric fistula presents three varieties, namely: (*a*) the blind internal subsphincteric fistula; (*b*) the complete subsphincteric fistula; and (*c*) the bilateral subsphincteric fistula.

(*a*) *The blind internal subsphincteric fistula* is the early stage of the complete variety and consists of an abscess cavity situated beneath the external sphincter muscle and communicating with the interior of the anal canal through an internal

opening which is the entrance to one of the Morgagnian sinuses. In those instances in which the source of infection is situated at the lower part of the anal canal—for instance in a fissure—the initial abscess is often situated between the superficial and the deep portions of the external sphincter muscle. In either situation the abscess eventually points at the outer border of the external sphincter, forming an exquisitely painful swelling associated with a discharge of pus from the anal canal.

(*b*) *The complete subsphincteric fistula* is a later stage of the preceding variety, the pus having found an exit through the skin at the outer border of the external sphincter. The external opening is situated about 1½ inches from the anal verge. Extension of the fistula, as the result of septic lymphangitis, takes place in the subcutaneous tissue, the off-shoots terminating in secondary openings. When the primary external opening is situated anteriorly to the transverse anal line the offshoots extend forwards and towards the middle line, but when the primary external opening is situated posteriorly to the transverse anal line the offshoots extend backwards and outwards.

The position of the internal opening and the direction taken by the main track towards it vary according to the position occupied by the primary external opening in reference to the transverse anal line. When the primary external opening is situated *anteriorly* to the transverse anal line or on that line, the internal opening is situated directly opposite to it in the same radial line, between the sphincters, and the main track adopts a straight course. When, however, the primary external opening is situated *posteriorly* to the tranverse anal line, the internal opening will be found in the middle line of the anal canal posteriorly, at the level of the interval between the sphincters, the main track taking a curved course backwards and inwards (fig. 20, opening behind B, p. 89). It is important to bear these points in mind when performing an operation for subsphincteric fistula.

(*c*) *The bilateral subsphincteric fistula* is due to subcutaneous offshoots, from the termination of the main track of a subsphincteric fistula, extending on both sides of the middle line in those instances in which the primary external opening is situated in front of the anus at or near to the middle line (fig. 21, A, B, H, p. 89). The bilateral disposition of the subcutaneous offshoots from a median subsphincteric fistula has given rise to the term "anterior horse-shoe fistula." Several secondary external openings may be present, but the primary external opening is always situated at the outer margin of the external sphincter, and the direction taken by the main track is straight beneath the muscle. The internal opening will be found opposite the interval between the sphincters, in the same radial line as the external opening.

Differential diagnosis.—Subsphincteric fistulæ can be distinguished from purely subcutaneous fistulæ by the fact that their main tracks, by passing beneath the external sphincter, cannot be palpated in the subcutaneous tissue. A perineal urethral fistula, however, exhibiting subcutaneous extensions in close proximity to the anus may resemble a subsphincteric fistula, in connection with which subcutaneous extensions may exist in front of the anus. Both fistulæ have their origin in a painful inflammatory swelling in front of the anus—near to the middle line—which increases in size and ultimately discharges through one or more external openings. The direction taken by the main track from the primary external opening is of great importance for the purpose of distinguishing between them. The main track of the urethral fistula extends forwards towards the scrotum, whereas that of the subsphincteric fistula extends towards the anus and passes beneath the external sphincter. The urethral fistula is invariably associated with a stricture of the urethra, the presence of which is easily ascertained by passing a sound. The absence of induration in the ischio-rectal fossa, as determined by palpating the tissue of the fossa between the finger in the rectum and the thumb externally, serves to differentiate the subsphincteric from the ischio-rectal or the para-rectal types.

Operative technique.—In those cases in which the external opening is situated at

the outer border of the external sphincter, either anteriorly to the transverse anal line or on that line, the main track is straight and takes a radial course to the internal opening which is situated between the sphincters. All that is necessary, therefore, is to introduce a probe-director into the primary external opening and pass it along the track until it protrudes through the internal opening and then to liberate the probe by dividing the tissues over it. The resulting incision is then extended for a short distance beyond the external opening, so as to provide for adequate drainage. The surface wound is also further increased in area by short relieving cuts made at right angles to the line of the main incision, on either side, through the skin and subcutaneous tissues. The presence of offshoots in the subcutaneous tissue should be sought for by careful probing and, if found, these should be laid open freely. In those cases in which the primary external opening is situated posteriorly to the transverse anal line and the main track curves backwards and inwards towards the middle line posteriorly, the method advocated for laying open the main track of a complete ischio-rectal fistula should be adopted. When operating upon a fistula of the subsphincteric type, careful search should always be made for either a submucous extension or a blind internal intermuscular fistula originating from the site of the internal opening, as these occasionally exist and, if overlooked, prevent complete healing.

After-treatment.—The wound resulting from laying open the subcutaneous offshoots in connection with a subsphincteric fistula needs very little attention, as it is superficial and should be treated on the lines suggested for a subcutaneous fistula. The portion of the wound, however, which extends through the external sphincter into the anal canal must be treated with particular care. The packing in this portion of the wound should be removed at the expiration of four days. Twice daily afterwards, and after each action of the bowels, the wound should be cleansed, but on no account should it be repacked. Repacking of the wound through the external sphincter ends in healing taking place with a depressed scar, which is one of the commonest causes of impairment of control over the contents of the rectum after operations for fistula. Should there be a tendency for the edges of the wound to adhere to one another, a thin layer of wool is all that is required to keep them apart. When treated in this way, healing takes place progressively from the deepest part of the wound and the resulting scar is not depressed. The duration of the healing process is generally from three to four weeks.

The Ischio-rectal Type of Ano-rectal Fistula.

The fatty tissue of the ischio-rectal fossa, being of low resisting power and exposed to pressure and contusions, is frequently the seat of an abscess which terminates in a fistula. The main track of the resulting ischio-rectal fistula is therefore confined to the ischio-rectal fossa. The abscess preceding the fistula is generally the result of septic lymphangitis extending from a septic focus situated in the posterior part of the anal canal, but occasionally it may be due to local infection by micro-organisms circulating in the blood-stream. The initial lesion is always situated in the anal canal posteriorly, between the sphincters. Whenever an ischio-rectal fistula is found to exist, there is invariably marked separation between the sphincters. Normally, the internal sphincter is so closely superimposed upon the external that it is difficult to determine exactly where one begins and the other ends, but when they are separated from one another a distinct sulcus, seldom exceeding one-third of an inch in extent, can be made out to exist between the muscles on introducing the finger into the anal canal. The separation is more pronounced in the middle line posteriorly than elsewhere. The separation between the muscles is produced by the levator ani contracting forcibly in an endeavour to overcome the limitation, imposed by the presence of the pecten band, to the normal expansion of the external sphincter during defæcation. Consequently the internal

sphincter is pulled away from the underlying external sphincter, and a sulcus between the muscles is formed. The mucosa in the middle line posteriorly, where the separation is widest, is apt to become abraded during the passage of a constipated stool, and then a septic focus is established. The resulting abscess discharges on the skin surface by an external opening, situated generally about two inches distant from the anal verge and slightly behind the transverse anal line. The main track of the fistula thus formed curves backwards along the course of the infected lymphatics towards the middle line and terminates in the middle line of the anal canal, opposite the interval between the sphincters, by means of an internal opening which is located at the site of the initial lesion. For these reasons the main track of an ischio-rectal fistula always takes a curved course backwards from the primary external opening (fig. 20, D, E, p. 89) and the internal opening is always situated in the middle line posteriorly between the sphincters and nowhere else. Owing to the symmetrical arrangement of the lymphatics, when the infection extends to the opposite side, the extension follows an exactly similar course as that taken by the original main track, with the result that the so-called posterior horse-shoe fistula is formed (fig. 25, p. 90).

There are four varieties of the ischio-rectal fistula, namely: (*a*) the blind external ischio-rectal; (*b*) the blind internal ischio-rectal; (*c*) the complete ischio-rectal; and (*d*) the bilateral ischio-rectal (posterior horse-shoe).

(*a*) *The blind external ischio-rectal fistula* is probably the only fistula which is not due to infection from within the rectum. Sitting upon a cold seat or riding upon a wet saddle may so reduce the vitality of the ischio-rectal fat that it readily falls a victim to any micro-organisms that may be circulating in the blood and becomes the seat of an abscess, much in the same way as a perinephric abscess develops as the result of blood infection from a septic focus elsewhere. The external opening of this variety of ischio-rectal fistula is usually situated about two inches distant from the anal verge, either in front of or behind the transverse anal line. The main track curves backwards towards the interval between the sphincters in the middle line, but there is no communication with the rectum (fig. 22, p. 89).

(*b*) *The blind internal ischio-rectal fistula* is always the result of infection from within the rectum. The initial lesion is either an abrasion of the mucosa, a fissure, a tear at the base of the pedicle of a fibrous polypus, or an ulcer in one of the large sinuses of Morgagni situated on either side of the middle line of the anal canal. The internal opening, which is often large, is situated in the middle line posteriorly between the sphincters (fig. 23, p. 89) and discharges pus freely. As there is no ternal opening, and as contraction of the external sphincter, occurring reflexly on account of the pain occasioned by the inflammatory process, prevents free escape of pus through the internal opening, this variety of ischio-rectal fistula is usually associated with the signs and symptoms of an acute ischio-rectal abscess.

(*c*) *The complete ischio-rectal fistula* is a later stage of the preceding variety. Extensions from the main track lead to the formation of multiple secondary external openings.

(*d*) *The bilateral ischio-rectal fistula* is the result of a septic lymphangitis extending to the opposite side from the original focus. This is more likely to occur when the internal opening of a blind internal or of a complete ischio-rectal fistula is exceptionally large, such as that produced by laceration of the pedicle of a fibrous polypus attached to a valve of Morgagni. Under such circumstances fæcal matter readily enters the main track of the fistula and sets up active suppuration. In consequence of this, numerous offshoots are formed which terminate in secondary external openings. In those instances of bilateral ischio-rectal fistulæ which have multiple secondary external openings on both sides, it is not uncommon to find that a deeply situated offshoot passes forwards beneath the inferior hæmorrhoidal vessels as they cross the ischio-rectal fossa, and terminates in an external opening in front of the anus close to the middle line. Should a similar offshoot exist on the

opposite side, the anus becomes surrounded by the fistulous track. A blind internal fistula may exist on one side and a complete fistula on the opposite side, or both of them may be complete and symmetrically disposed in regard to the course taken by the main tracks (fig. 25, A, B, p. 90). Even when several secondary external openings exist on both sides, there is never more than one internal opening present, which is situated in the middle line posteriorly between the sphincters (fig. 25, D).

Differential diagnosis.—The characteristic features of a complete ischio-rectal fistula are: (1) the primary external opening is situated posteriorly to the transverse anal line and at a greater distance than an inch and a half from the anal verge; (2) the internal opening is always in the middle line posteriorly, at the level of the interval between the internal and external sphincters; and (3) the induration is confined to the ischio-rectal fossa and does not extend above the level of the levator ani.

The position of the primary external opening serves to distinguish the ischio-rectal fistula from the submucous, the subsphincteric, and the retro-rectal, because each differs in regard to its distance from the anal verge. The primary external openings, of the para-rectal and the pelvi-rectal fistulæ, however, occupy a similar position to that of the ischio-rectal, so that the diagnosis rests upon the direction taken by the main track and the position of the internal opening. The main track of an ischio-rectal fistula pursues a course parallel to the skin surface, curving backwards towards the middle line, and terminates at an internal opening situated in the middle line between the sphincters. The main tracks of the para-rectal and the pelvi-rectal fistulæ are parallel to the longitudinal axis of the rectum and extend deeply into the pelvis for a distance of several inches.

Clinical course.—So long as the primary external opening of an ischio-rectal fistula remains patent and the internal opening is small, the formation of offshoots from the main track is not likely to take place. When, however, the internal opening is large, fæcal matter is apt to find its way into the main track and set up active inflammation, so that secondary abscesses are formed which discharge their contents through secondary openings upon the skin surface. Moreover, infection of the lymphatic channels of the opposite ischio-rectal fossa may ensue and lead to the development of an ischio-rectal fistula on that side. On account of the symmetrical disposition of the lymphatics, the resulting fistula is a replica of the original fistula and communicates with it by means of a track which passes beneath the ano-coccygeal ligament.

Operative technique.—A blind external ischio-rectal fistula may, in some instances, be cured by laying open the main track from the external opening as far as its blind extremity, together with any offshoots that may exist, and then increasing the surface area of the wound to a suitable extent by means of relieving cuts. If, however, the blind end of the track passes beneath the external sphincter muscle so that mucous membrane only intervenes between it and the anal canal, time will be saved by converting the blind external fistula into a complete fistula, by forcing the point of a probe-director through the mucosa between the sphincters and then liberating the director by dividing the tissues covering it.

When operating upon a blind internal ischio-rectal fistula, the exact position and extent of the main track should be ascertained by introducing the finger into the rectum and palpating the ischio-rectal fossa between it and the thumb placed upon the skin surface. An incision is then made into the indurated area (occasionally fluctuant if active suppuration is progressing) radiating outwards, as shown in fig. 17, p. 88, to the required extent, and then the main track is laid open in accordance with the method advised for a complete ischio-rectal fistula. When the fistula has become complete, the primary external opening indicates the surface termination of the main track, so that, in order to ensure that the main track is laid open, the probe-director should be introduced into the primary opening and not into a secondary opening if

one exists. Since the main track of a complete ischio-rectal fistula always takes a curved course backwards towards the internal opening (fig. 20, D or E, p. 89) it is not possible to introduce the probe-director far enough along it in order to reach the internal opening, on account of the bend in its course. The probe-director should, therefore, be gently passed along the track as far as it will go, and when it is found that further progress is impeded, it should be forced through the skin at that point. The overlying tissues are divided and then the probe-director is re-introduced as far as it will go and again forced through the skin if it does not readily reach the internal opening. After dividing the overlying tissues, if a portion of the track still remains undisclosed, the above manœuvre is repeated until the point of the probe protrudes through the internal opening. When the main track has thus been completely exposed from end to end, the surface area of the wound shonld be increased by making relieving cuts at points where there is most tension on the edges of the main incision. A careful search is then made for offshoots from the main track. Superficial offshoots should be laid open freely from end to end, but when a deep offshoot is discovered, extending forwards beneath the inferior hæmorrhoidal vessels, it should not be laid open as, by so doing, the nerve supply of two-thirds of the external sphincter would be cut off, and some measure of incontinence will result. Under such circumstances, the portions of the offshoot behind and in front of the vessels should be laid open, but the part beneath them must be kept intact. When operating upon a bilateral ischio-rectal fistula (posterior horseshoe) all the existing tracks on both sides, as well as the track passing beneath the ano-coccygeal ligament, should be laid open completely, but the part of the main track, which passes beneath the external sphincter to the internal opening, should not be laid open until the greater part of the wound has been filled in. Lastly, a careful search should always be made for a submucous extension above the internal opening (fig. 26, p. 90).

After-treatment.—The after-care of an ischio-rectal fistula is practically identical with that of a para-rectal fistula. The packing in the wound is removed on the fifth day and the wound cavity is thoroughly irrigated with a strong antiseptic solution. Surfaces of the wound, which tend to make contact with one another, should be kept apart by inserting a thin layer of cotton-wool between them. On no account should the cavity of the wound be repacked. At the expiration of ten days after the operation, the surface of the wound will usually be found to be covered by healthy granulations and there should not be any appreciable purulent discharge. Should pus collect in the wound, it should be regarded as evidence that active suppuration is taking place somewhere in the neighbourhood and, accordingly, a careful search should be made for offshoots from the main track of the fistula, which may have escaped detection when the operation was being performed or had developed subsequently. There are three situations where search should always be made under such circumstances, namely : (1) posteriorly, for a track extending to the opposite side beneath the ano-coccygeal ligament ; (2) anteriorly, for a track passing forwards and inwards beneath the inferior hæmorrhoidal vessels ; and (3) for a track extending upwards beneath the mucosa from the site of the internal opening, which is always situated in the middle line posteriorly, between the sphincters. As soon as the presence of an actively suppurating track has been disclosed, immediate steps should be taken to deal with it so as to prevent further extension. Thus, when an offshoot is found to extend to the opposite side, it should be laid open completely from end to end, relieving cuts being made at suitable points along the edges of the resulting wound. In the event of a submucous extension being discovered, the method recommended for dealing with a submucous fistula should be adopted. When, however, a track is found extending beneath the inferior hæmorrhoidal vessels, it should not be laid open completely to the skin surface, because the nerve supply of the anterior two-thirds of the external sphincter muscle would thereby be destroyed. A small crucial incision should, therefore, be

made over the anterior extremity of the track, in order to provide a free exit for the pus, and then the portion of the track passing beneath the vessels should be thoroughly cauterized with nitrate of silver. Several such applications may be necessary, at intervals of three or four days, before the track beneath the vessels is obliterated.

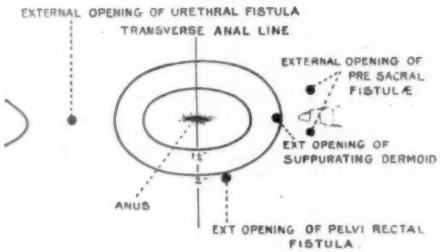

EXTERNAL OPENING OF URETHRAL FISTULA
TRANSVERSE ANAL LINE
EXTERNAL OPENING OF PRE SACRAL FISTULÆ
EXT OPENING OF SUPPURATING DERMOID
ANUS
EXT OPENING OF PELVI RECTAL FISTULA

FIG. 1.—Showing the position of surface openings of fistulæ having no connection with the rectum.

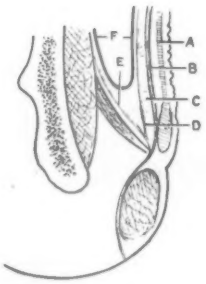


FIG. 2.

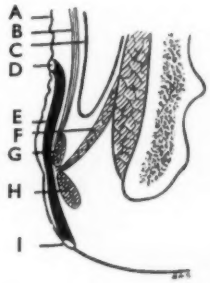


FIG. 3.

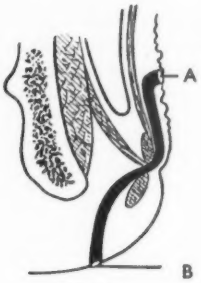
FIG. 2.—Showing the pelvi-rectal and para-rectal spaces.[1]

A—External muscular coat. B—Internal muscular coat. C—Para-rectal space. D—Fascia propria. E—Pelvic fascia. F—Peritoneum.

FIG. 3.—Complete submucous fistula.

A—Mucosa. B—Muscular coat. C—Pelvic peritoneum. D—High-lying internal opening of fistula. E—Main track of fistula. F—Levator ani. G—Internal sphincter. H—External sphincter. I—External opening.

[1] The blocks for figures 2 to 10, 13 to 18, and 20 to 26 were kindly lent by the Editors of the *Practitioner*.



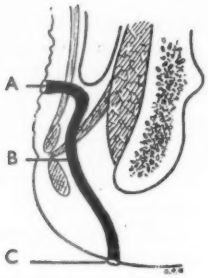


FIG. 4. FIG. 5.

FIG. 4.—Ischio-rectal fistula with submucous extension.
A—Internal opening. B—External opening.

FIG. 5.—Complete para-rectal fistula.
A—Internal opening. B—Main track. C—External opening.

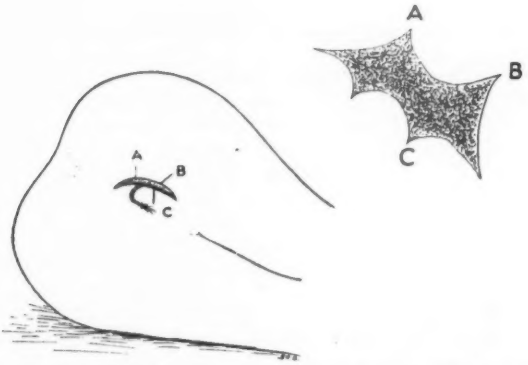
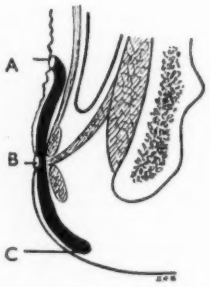
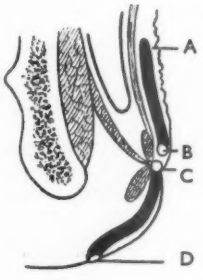


FIG. 6.—Showing relieving cuts, A, B and C, along margins of linear wound.
Inset.—Showing increase of surface area resulting from incisions at A, B and C.





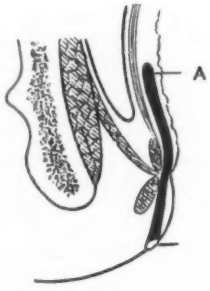


FIG. 7. FIG. 8. FIG. 9.

FIG. 7.—Blind internal subcutaneous fistula and complete submucous fistula having an internal opening in a fissure.

FIG. 8.—Complete subcutaneous fistula with submucous extension resulting from a fissure.

FIG. 9.—Blind external submucous fistula. A—Cul-de-sac of submucous track.

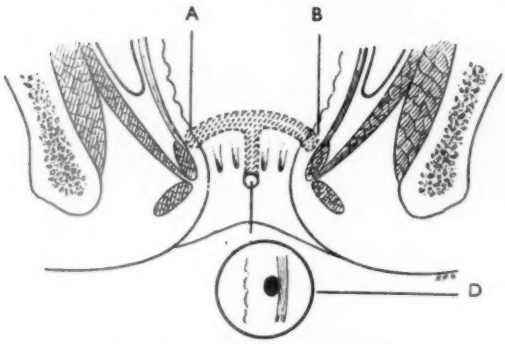


FIG. 10.—Bilateral submucous fistula.

Inset. D.—Showing the position of the track in regard to the muscular coat of the rectum.

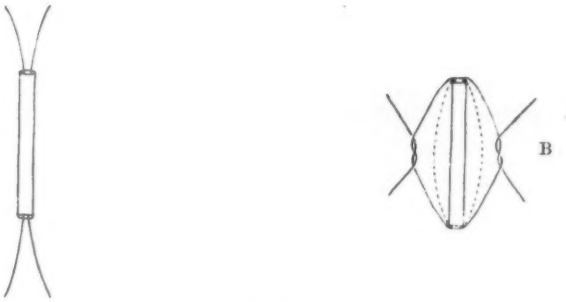


FIG. 11.

FIG. 11.—The ligature method of treating a submucous fistula.

A—A double ligature introduced into the main track. B—The area between the dotted lines indicates the granulating surface left after the ligatures have separated.

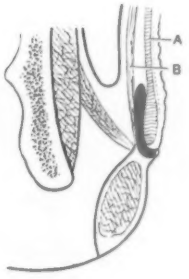


FIG. 12.

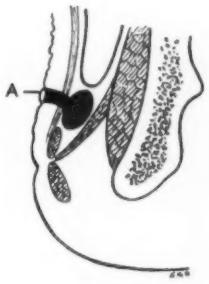


FIG. 13.

FIG. 12.—A blind internal intermuscular fistula. Note that the main track lies externally to the internal sphincter muscle.

FIG. 13.—First stage of a para-rectal fistula. A.—The internal opening.

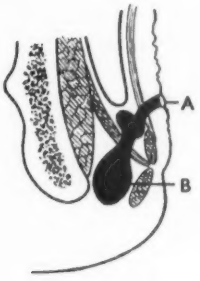


FIG. 14.

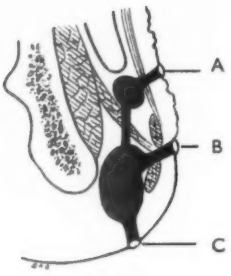


FIG. 15.

FIG. 14.—A para-rectal fistula extending into the ischio-rectal fossa.

FIG. 15.—A complete para-rectal fistula. A—Primary internal opening. B—Secondary internal opening. C—Primary external opening.

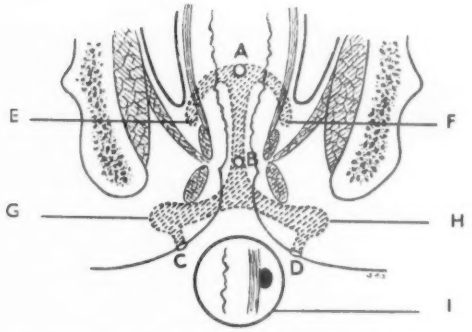


FIG. 16.—A bilateral para-rectal fistula. E and F indicate the blind extremities of the track above the level of the levatores ani.

Inset.—Showing the main track external to the muscular coat of the rectum.

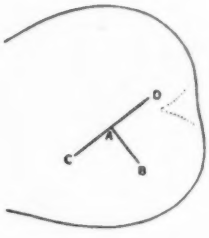


FIG. 17.

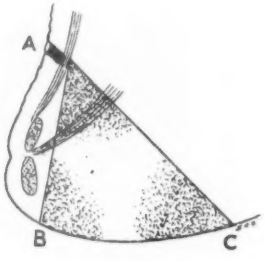


FIG. 18.

FIG. 17.—Showing the incisions recommended when operating upon a para-rectal fistula.

FIG. 18.—Showing the wound resulting from the incisions indicated in fig. 17. Note that the wound extends as far as the external muscular coat of the rectum but *not* through it.

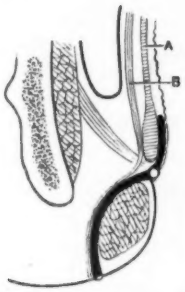


FIG. 19.—Complete subsphincteric fistula with submucous extension. Note that the main track is situated between the muscle and the expansion from the external coat.

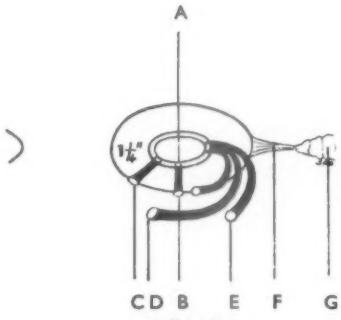


FIG. 20.

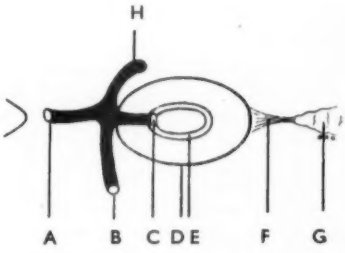


FIG. 21.

FIG. 20.—Showing the relation of the external opening to the internal opening in subsphincteric and ischio-rectal fistulæ. F.—Ano-coccygeal ligament. G.—Coccyx.

FIG. 21.—A bilateral subsphincteric fistula. (Anterior horse-shoe.

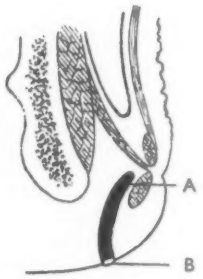


FIG. 22.

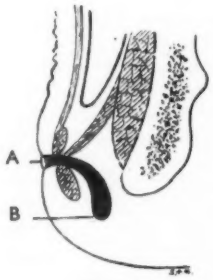


FIG. 23.

FIG. 24.

FIG. 22.—A blind external ischio-rectal fistula. A.—The blind extremity pointing towards the interval between the sphincters.

FIG. 23.—A blind internal ischio-rectal fistula. B.—The blind extremity approaching the skin surface.

FIG. 24.—A complete ischio-rectal fistula.

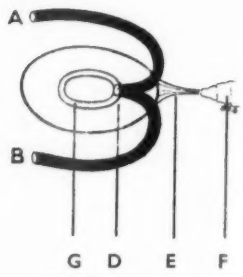


FIG. 25

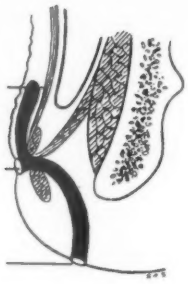


FIG. 26.

FIG. 25.—A complete bilateral ischio-rectal fistula. Note that there is only one internal opening. C.—Interval between sphincters. D.—Internal opening. E.—Ano-coccygeal ligament. F.—Coccyx.

FIG. 26.—A complete ischio-rectal fistula, with a submucous extension terminating in a cul-de-sac.

Section of Urology.

President—Mr. RALPH THOMPSON, Ch.M.

[*April* 28, 1932.]

Bilateral Transplantation of Ureters and Colostomy for Vesico-vaginal and Vesico-rectal Fistulæ.—HAROLD DODD, F.R.C.S.

IN February, 1927, this patient had a uterine hæmorrhage, for which a radium application was made. Four months later the bleeding recurred, and a further examination revealed a carcinoma of the cervix. Radium was again applied and, the following week a panhysterectomy was performed. The patient was discharged a fortnight later with a six weeks' expectation of life, and soon afterwards she had urinary and fæcal fistulæ into the vagina. She continued with this double leak, in comparatively fair health and comfort, for nearly two years.

In November, 1929, she was readmitted to hospital, and an unsuccessful attempt was made to close the fistulæ. She returned home a month later, much worse.

She now lived in misery, caused by a severe excoriation of the skin of the lower abdomen, perineum, and thighs. I was asked to see her on February 4, 1930. The atmosphere of the room was indescribable, it being a mixture of decomposing urine and fæces, with which the bed was soaked. She was reduced to a moaning, feeble, cadaverous being, crying to be relieved of her pain or to be given something that she might die. She had an acute pustular dermatitis from the umbilicus to below the knees, and was having a steadily increasing amount of morphia daily. She and her husband repeatedly implored the doctor to "end it."

She was admitted to the King George Hospital, Ilford, on February 6, 1930, and on examination I found a "three-finger" vesico-vaginal fistula, and a "one-and-a-half-finger" recto-vesical fistula, the edges being thick, rigid, and of cartilaginous hardness. There was no sign of growth locally (fig. 1).

I performed a left inguinal colostomy immediately, and this relieved her a little for four or five days when, feeling better, she began to eat, and complained of a return of the pain, whilst the ward sister reported the passing of fæcal material through the vagina. As the colostomy was working well, the source of the fæcal matter could not be the colon; was there a further intestinal leak? She was given a meal of currants, and some of them appeared at the vagina in an hour's time, thus establishing the existence of a small intestine fistula, and explaining the cause of the painful excoriation; it was a digestive action.

Further operation was advised, but she declined it and went home. A fortnight later she returned, no better, having decided to accept the treatment in the hope of improvement or that she would "pass out" during it.

Skiagrams of the thorax, spine, and pelvis showed no sign of secondary deposits.

The bladder fistula was so large, hard, and fixed that I considered it irreparable, and I decided on transplantation of the ureters into the colon above the colostomy.

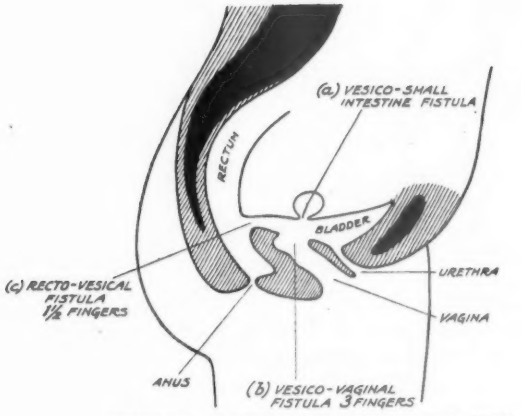

(a) VESICO-SMALL INTESTINE FISTULA
RECTUM
BLADDER
URETHRA
VAGINA
(c) RECTO-VESICAL FISTULA 1½ FINGERS
ANUS
(b) VESICO-VAGINAL FISTULA 3 FINGERS
CONDITION WHEN FIRST SEEN FEB. 1930.

FIG. 1.

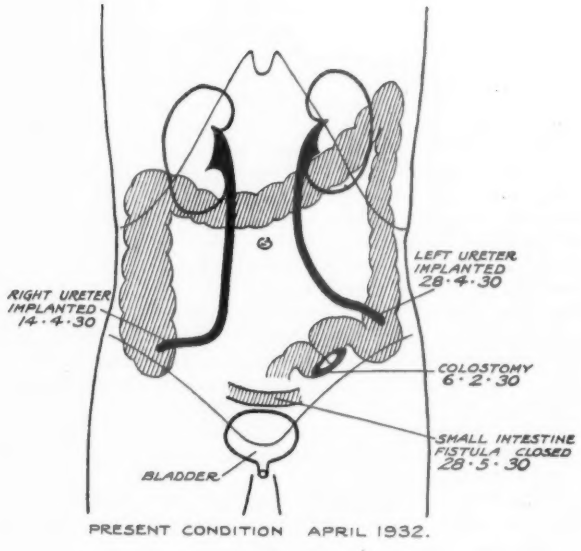

LEFT URETER IMPLANTED 28·4·30
RIGHT URETER IMPLANTED 14·4·30
COLOSTOMY 6·2·30
SMALL INTESTINE FISTULA CLOSED 28·5·30
BLADDER
PRESENT CONDITION APRIL 1932.

FIG. 2.

On April 14, I placed the right ureter into the upper part of the cæcum, and a fortnight later implanted the left one into the descending colon.

She was still very depressed, and in spite of careful tight packing of the vagina and dieting, the irritating digestive action of the small intestine leak continued on the perineum and thighs.

On May 25, I explored the abdomen and found an ileo-vesical fistula. There were no signs whatever of secondary malignant deposits in the abdomen. I separated the ileum from the bladder and closed the resulting openings. The patient made an uneventful recovery. Fig. 2 shows her "re-arrangement."

She left the hospital at the end of June fitted with a combined colostomy-urinal belt, which worked adequately. Since then she has put on two stones in weight, and the belt fits better than at first, when she was so emaciated. She is able to do her lighter home duties and shopping. She was heard to say, in the out-patient department, that she was tired, after walking there from her home which was three miles away!

I have seen her six-monthly since. She continues in good health. At first, her real difficulty was to manage the urinal whilst in bed, in order to keep dry; experience has overcome this to a large extent.

May, 1932.—An "abrodil" excretion pyelogram reveals that the right kidney is now slightly damaged, although clinically she has no symptoms. Dr. Rhynland Parry's report reads as follows:—

"9.9.32.—The right kidney appears to be low in position and the upper end of the ureter is dilated, the left kidney is also low, there does not appear to be any abnormality in the formation of the calyces except the dilatation of the pelvis in the right kidney. The right ureter terminates in the region of the cæcum. There is an opacity in the region of the cæcum, which would suggest the presence of abrodil, and likewise an opacity in the region of the pelvic colon, suggesting the presence of abrodil in the bowel."

The pelvic floor has softened to approaching normal consistency.

This case is interesting, showing as it does:—

(1) A serious debilitating complication after the application of radium, even though that has probably cured the cancer.

(2) That by a colostomy and implantation of the ureters into the cæcum and descending colon, patients who would otherwise be miserable human "derelicts," can be returned to fair health and a useful life.

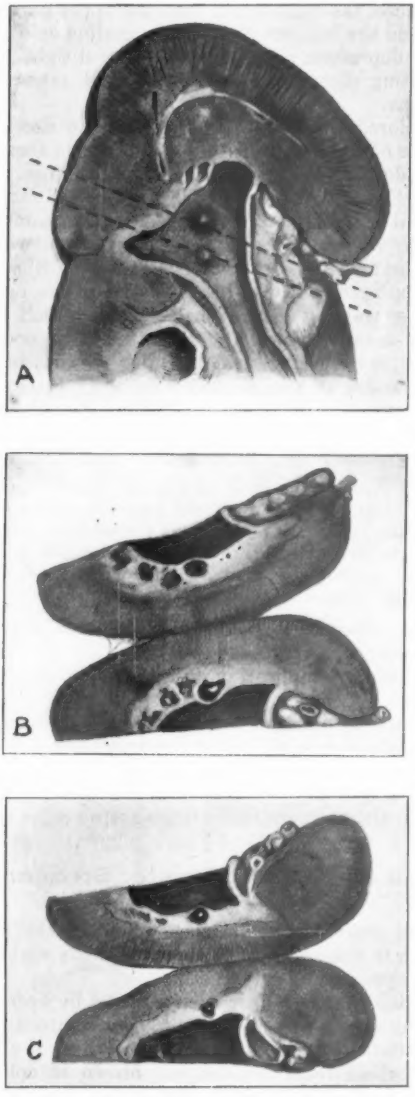
(3) That infection is probably taking place on the right side, from the septic contents of the cæcum, although clinically there are no signs of it.

Calculi formed in the Renal Substance: Specimen.—H. P. WINSBURY-WHITE, F.R.C.S.

This specimen is of great interest because it shows the presence of stones in a most unusual situation in the kidney. They are actually embedded in the substance in the vicinity of the upper group of calyces.

The specimen is a left kidney which was removed by operation from a man aged 29. The corresponding ureter was dilated and opened into a vesical diverticulum.

On examining the hardened specimen, one noted first of all the dilated condition of the calyces. The whole renal mucosa was brown in colour from inflammation and some interstitial change was noted throughout the renal substance. In the floor of the dilated upper calyx my attention was attracted by two slight prominences. The mucosa over these points was intact. On touching them with the point of a knife, it became certain that there were concretions beneath. Two transverse cuts across these areas revealed the fact that in the renal substance, adjacent to the mucous membrane, were two small cavities, in each of which were two stones. The calculi were hard and black, and ranged in size from that of a pin-head to that of the head of a match.



Stones formed in renal substance of left kidney. Left megalo-ureter opened into a vesical diverticulum.

Adjacent to the cavities containing the stones were two small areas of disintegrating renal tissues. These gave the impression that the cavities containing the stones arose from a similar local breaking-down of renal substance. Microscopically these areas were seen to be small zones of inflammation surrounded by disorganized renal tissue.

A report from Eastes' Laboratory on the chemical composition of the smallest stone, stated that it consisted of calcium oxalate.

Considering all the facts of this case, we have the following sequence of phenomena: (1) obstruction at the lower end of the ureter, with dilatation of this structure and of the renal calyces; (2) supervening infection and necrosis of kidney tissue leading to (3) cavity and stone formation.

Hydonephrosis with inadequate Ureter. Specimen.—H. P. WINSBURY-WHITE, F.R.C.S.

With regard to the pelvic type of hydronephrosis, we are able to separate these cases into groups which show different forms of obstruction.

There is the group in which the kinked upper part of the ureter is adherent to the pelvis. I regard the adhesion between these two structures as the cause of the obstruction. There is no reason why a valve-like opening of the pelvis into the ureter should not be regarded merely as an advanced stage of this condition. Secondly there is the too narrow opening of the pelvis into the ureter, without any kinking. There is the group in which no obstruction at all can be found; the opening into the ureter, and even the ureter itself, may be dilated. There is also the group in which a narrowing of a certain length of the ureter is present; the case which I am presenting fits into this group.

The lumen of the uppermost two inches of the ureter was so small that an ordinary probe could not be passed down it. There is nothing of any special interest in the clinical features of the case. The patient was a man aged 43 who had for some months been conscious of a lump in the right side. I removed the kidney, which contained about a quart of urine. The convalescence was uneventful.

Hydronephrosis with Secondary Calculi: Specimen.—H. P. WINSBURY-WHITE, F.R.C.S.

This is a left kidney which I removed from a boy aged 5 years. He made a good recovery from the operation. His complaint was passing blood in the water intermittently for a period of two years. The only pathological element found in the urine was a certain amount of albumin. The stones showed clearly in a skiagram.

The specimen shows the usual characters of a pelvic hydronephrosis. There is a definite narrowing of the ureter at its commencement.

Eight rounded stones, light brown in colour and about the size of dried peas, are seen in the pelvis. There are two special points of interest in this case. One is that from the preliminary skiagram one was able to assume, from the rounded character of the stones, that they lay in a dilated portion of the kidney where they had a considerable range of movement. The other point important to emphasize is that, in carrying out the treatment it is useless to remove the stones and to leave behind the predisposing cause, which is bound to give rise to further calculous formation. It was for this reason that nephrectomy was carried out in this case.

Ureterogram of a Case of Valvular Obstruction at the Lower End of the Left Ureter, in a boy aged 12.—JOHN EVERIDGE, F.R.C.S.

Valvular obstruction at the uretero-vesical orifice is a rarity. That this is a case of that condition appears to be beyond doubt.

The history and progress are as follows: Eighteen months ago, hæmaturia occurred. This has reappeared three times since. I first saw the case on January 7,

1932, and advised cystoscopy. This, with catheterization of the ureters, I carried out on February 4, 1932, with negative results. No definite explanation of the bleeding having so far come to light, I carried out intravenous pyelography, on February 14, and by that means a left hydronephrosis and a left hydro-ureter were revealed. Instrumental ureterography (sodium iodide, 13·5%) more thoroughly demonstrated the hydroureter. The diagnosis thus lay between a transparent stone or a valve. Cystoscopy had excluded a diverticulum of the bladder compressing the ureter.

Instrumental ureterogram, showing dilated ureter due to ? valvular obstruction.

Three weeks ago, April 4, 1932, I operated and found the ureter dilated to the size of the small intestine. This was traced down to the bladder extra-peritoneally but no stone was discovered. On opening, a probe passed easily up to the kidney but was checked at the bladder entrance. The incision in the ureter was carried down to the bladder. The bladder was then opened and a ureteric catheter passed up the ureter. The ureteric orifice was incised upwards and outwards, the hole thus made in the bladder admitting the finger. With interrupted sutures, this hole was anastomosed to the margins of the ureter incision, leaving a uretero-vesical orifice of over half an inch in diameter.

I call this case one of valve of the ureteral orifice, as I do not see what else it could be. It was clearly not one of stenosis—which is common enough—since ureteral catheterization never presented difficulty.

Diverticulum of the Male Urethra associated with Diverticulum of the Bladder.—W. K. IRWIN, F.R.C.S.

Patient, A. S., aged 19, began to have frequency of micturition in January, 1928. Four months later the tubercle bacillus was demonstrated in his urine.

He has suffered from urinary incontinence since November, 1930. About a year ago he noticed that pressure in the left scrotal region caused urine to dribble away. Two months ago he felt a small scrotal "lump" which has gradually increased in size. No history of urethral obstruction or discharge.

Present condition.—A swelling about the size of a hen's egg is felt in the left side of the scrotum. It is tender and fluctuating, and urine, which is alkaline and ammoniacal, can be expressed from the external meatus. When the diverticulum is

emptied, the wall of the sac is felt to be well defined and uniformly smooth. On rectal examination, a large swelling, which is elongated and fluctuating, can be felt in the centre and on the right side. Cystoscopic examination demonstrates the opening of a diverticulum on the right lateral wall near the ureteric orifice.

X-ray examination—after the injection of an iodide solution into the urethra and vesical cavity—and excretion urography show a small bladder and, posteriorly and below it, a diverticulum, while a second diverticulum is seen to come off from the urethra.

Carcinoma of the Kidney. Specimen.—E. W. RICHES, M.S.

Removed by transperitoneal nephrectomy from a man aged 49. History of hæmaturia for 10 months. The specimen weighs 8 lb. 6 oz., and section showed a clear-celled tubular carcinoma.

The patient is now present (five months after operation).

Anomalous Kidneys. Specimens.—E. W. RICHES, M.S.

The patient was a man aged 56. The left kidney contains a hypernephroma at its lower pole, and in each kidney the ureter descends on the outer side of the kidney. One year before the left renal tumour was palpable, he had a pulsating tumour of the right humerus where there was a secondary deposit of new growth. Pigment is present in the sections of the hypernephroma and of the humerus.

[*May* 26, 1932.]

Perinephric Inflammation.

By H. P. WINSBURY-WHITE, F.R.C.S.

THE study of this subject raises some interesting points.

First of all, that the seat of infection which gives rise to pus in the perinephric tissues is commonly the adjacent renal cortex is a view that has been so well supported by anatomical findings that it is now generally accepted. The contention that a perinephric abscess originates in the tissue surrounding the kidney is a theory which has little more to support it than the fact that the evidence in the urine of renal infection is sometimes either extremely scanty or entirely lacking. It is a matter of personal experience—and a host of case reports in the literature show—that such urinary findings often accompany a focus of renal infection.

Another point of special interest is the frequency with which the renal infection is associated with a recent—or an existing—infection in some other part of the body. In contrast with this, in many cases no likely source of the infection can be found.

Because certain cases of perinephric abscess are associated with hæmaturia of renal origin, and because other cases of hæmaturia are associated with the same ætiological factors that are found commonly with perinephric abscess, one may regard these different cases as varying clinical types of the same disease.

Finally, the evidence on which to diagnose the presence of perinephric abscess, without waiting for a palpable tumour in the loin, is of great practical interest.

My own clinical observations result from a personal experience of ten cases of perinephric abscess which supervened on the following conditions: (1) pneumonia in a girl aged 4; (2) tonsillitis in a girl aged 8; (3) sore throat and a fall in a girl

aged 12; (4) recurring skin trouble in a youth aged 18; (5) direct injury to the kidney in a woman aged 20; (6) closed renal tuberculosis in a man aged 20; (7) closed renal tuberculosis in a woman aged 42; (8) bilateral renal calculus following pyelolithotomy on the left side in a boy aged 8; (9) long-standing renal calculi in a woman aged 58; (10) long-standing renal calculi in a woman aged 66.

Ætiology and Pathology.

The disease is noted somewhat more commonly in males than in females. This is in accordance with the greater liability of the former sex to boils and skin lesions generally, and to trauma. It may occur at any time of life, from infancy onwards, but in the great majority it arises in the second and third decades.

The right and left sides are involved with equal frequency. Blumenthal [1], who reviewed 1,500 cases in the literature, found no appreciable difference in the incidence on either side. Bilateral perinephric abscess is rare. The same author found it in only 2% of cases.

Chronic kidney disease.—With regard to predisposing pathological conditions, first of all, there are those cases in which the perinephric infection is but a complication of chronic disease of the kidney, such as pyonephrosis, calculus or tuberculosis. Four of my own cases came under this heading. Exceptionally in this group, the extra-renal complication may be the first important intimation of renal disease. Case 6 of my series falls into this class. More usually there is a previous history of symptoms related to the kidneys. The origin of the abscess in these circumstances is not obscure, and usually there is additional proof of renal involvement by the presence of pus in the urine. We need not concern ourselves further, therefore, with discussing the ætiology of this group of cases (Cases 7 and 10).

A distant focus of sepsis.—Next we come to those cases in which there is a definite recent history of a focus of sepsis in some other part of the body. This association occurs so commonly that it leaves no doubt as to the relationship of the two widely separated lesions. Skin diseases—especially boils—otitis media, pneumonia, septic tonsils, osteomyelitis, all figure in their turn in the antecedent history. Also in the same group are those in which the renal lesion follows a less localized infection, such as influenza, typhoid, chicken-pox and scarlet fever. One very unusual type of case has been reported [2]. An infant suckled at a breast which was the seat of an abscess, developed first of all stomatitis and later perinephric abscess.

Traumatism.—Traumatism recently received in the kidney region occasionally plays an important part in precipitating the infection. It is not always necessary that the kidney itself be injured, but extravasation of blood either from the adjacent abdominal wall or from the perinephric tissue is enough to lead to abscess formation. Blumenthal reports 12% of cases following trauma. It must be apparent that injury may be the precipitating cause, where predisposing sepsis already exists (Cases 3 and 5).

Brewer's [3] experimental work showed that animals with artificial trauma to the kidney had the greater incidence of cortical abscess on the injured side, following injection of staphylococci into the circulation.

Rupture from direct violence to a kidney of which the pelvis and calyces are filled with urine, causes an explosive injury from hydraulic force. When this occurs, there is bound to be some extravasation of urine. One observer reported a torn pelvis in 40% of 32 examples of injured kidney examined post mortem. There must be a considerable number of cases in which one or more of the calyces are involved in the tear in the renal substance; when we consider how widely distributed these are, it seems inevitable that there must be at least a small escape of urine outside the kidney. Judging by the fact that the great majority make a complete recovery on expectant treatment, it becomes apparent that this leakage is only slight. Any

considerable degree of continued escape of urine must, however, eventually give rise to infection. Case 5 of my own series belongs to the group of perinephric infection following direct violence to the kidney.

Perinephric infection following operations on the kidney.—This forms a group of cases which has special features. There is an escape of urine, either through a nephrotomy or a pyelotomy wound. Drainage by tube placed in the wound down to the site of the kidney incision, is not always a complete safeguard. This is because urine which escapes from the kidney tends to gravitate downwards around the ureter in the surrounding loose fatty tissue. This lies within the fascial sheath, which after closely enveloping the kidney deep to the perinephric fat then passes downwards, forming a wide covering for the peri-ureteral tissue. I am sure we have all had experience of pyelotomy or nephrotomy cases which during the convalescence develop tenderness along the line of the upper half of the ureter. Fortunately in most of these the inflammatory symptoms disappear in due course, but occasionally they progress to the formation of pus, which may then extend upwards to the renal fossa (Case 8).

The ascending route of infection in perinephric abscess.—Numbers of cases have been reported showing that perinephric abscess has followed acute infection of the genital and lower urinary tracts. In the female, uterine and tubal infection, and in the male, urethritis have been the most common antecedents (Miller [4]). According to Israel, the chief ætiological factor in 14 % per cent. of cases of perinephric abscess is gonorrhœa.

Those following parturition are especially interesting. One writer [5] reported three cases which occurred in his own practice during two years. Another writer (Hirst quoted by Miller) reported a case following abortion. It is of interest at this stage to make some reference to the lymphatic drainage from the genital organs to the lateral lumbar lymph nodes. These latter receive the drainage either directly or indirectly through the iliac and inguinal glands, from the bladder, testicles, penis and prostate, or from the clitoris, portions of the vagina, and uterus.

The anterior layer of renal fascia which encloses the perinephric fatty capsule passes in front of the lumbar glands, so that these lie in the same fascial plane as the perinephric fat. As abscess formation is such a well-known complication of adenitis in other parts of the body—for example, the neck, axilla, and inguinal regions—it is reasonable to assume that infection in the lateral lumbar nodes can likewise terminate in the same way. The lymph drainage from the appendix, gall-bladder, pancreas, spleen, and colon being into the median lumbar glands, traverses a route relatively remote from the adipose capsule and gives rise to subphrenic rather than perinephric abscess.

The cellular tissue of the true pelvis is closely connected with the kidney and the perinephric cellular tissue, through the lymphatic system. To my mind this explains many of those cases of chronic pelvic disease with pain in the kidney regions. It also calls attention to the fact that in many cases of pain in the renal area the origin of the symptoms may be the pelvic organs, which are quite unsuspected.

When a perinephric abscess is found to follow on some infective condition of the lower urinary tract—such as prostatitis, or a peri-urethral abscess—and autopsy investigation shows that the abscess cavity is confined to the perirenal sac, and no evidence can be found that the infection has come from the kidney, the presumption that the spread is a lymphatic one seems justified. Henry Morris [6] quoted, amongst other causes, the condition as following operations involving the scrotum, such as castration, the injection of a hydrocele, and excision of varicocele. It seems, therefore, that the case for the upward lymphatic spread is strongly supported. Morrissey [7] quotes a case following a punch operation on the vesical neck, in which perinephric abscess developed which did not involve the kidney. On the other hand, direct extension upwards to the renal fossa, of pus originating on the pelvic floor, definitely accounts for another type of the condition.

The kidney lesion.—We will now consider the nature and situation of the kidney lesion which leads to the perinephric collection of pus.

Abundant evidence has been forthcoming, both from the operating theatre and the post-mortem room, as to the nature of the renal lesions which produce the perinephric abscess. The following types have all been described :—

(1) Small abscesses which rupture on to the surface of the kidney. Evidence that some have healed while others are active is often forthcoming when the kidney is inspected. (2) A single abscess may become encysted in the kidney and eventually rupture. (3) A small area of infection showing points of suppuration which coalesce to form a single abscess which ruptures. (4) Diffuse suppuration nephritis. (5) An infarct which has gone on to suppuration.

The evidence available when a perinephric abscess is drained, that the infection originated in the adjacent renal substance, is sometimes strikingly confirmatory. For example, a necrotic renal area is identified either with the finger, when it can often be shelled out, or by inspection when the kidney is removed, or merely brought out on to the loin. On the other hand, when a large perinephric abscess is opened, the walls of the cavity may be so well covered with granulation tissue that it is quite impossible to identify any part of the kidney.

Such an experience is apt to be regarded as supporting the view that the origin of the abscess is extra-renal, especially when the urinary findings in the case show no evidence of renal infection.

I recently dealt with a case (4) which presented all these features, and I should have been quite unable to offer proof that the suppuration had originated in the kidney, had I not found a piece of tissue about two inches in diameter which I detached with my finger from the surrounding wall of the abscess cavity. This proved on microscopic examination to be kidney substance and fat. Evidently a localized renal abscess had caused a slough of part of the cortex.

Quite commonly pus escapes into the perinephric tissue from a septic focus in the kidney without being suspected. Aschner, in reviewing the records of staphylococcal infection of the kidney in the Mount Sinai Hospital, found, in addition to thirty-six cases of perinephric abscess, seventeen of renal infection which had given rise to some perinephric pus. Decapsulation sometimes reveals cortical abscesses which might otherwise be missed.

The spontaneous resolution of perinephric infection of renal origin is evident from the presence on the kidney surface of scars of recently healed inflammatory foci accompanied by extensive fibro-lipomatous perinephric change with dense adhesions to the true capsule (fig. 1, p. 59).

The causal organism.—The bacteria found in the urine do not necessarily represent those which initiated the renal lesion. The tendency of the *Bacillus coli* to establish itself in a focus already caused by an organism of a different nature, is well known, and has been the chief cause of difficulty in establishing bacterial responsibility. This organism, indeed, seems to be an inevitable visitor to the urinary tract consequent upon any chronic pathological condition which occurs there.

Mention has already been made of the fact that a peripheral lesion may be identified as the initiating cause of the renal complication. Nevertheless bacteriological proof of the association of the two conditions is often lacking. Perhaps the commonest and best instances of this difficulty are exemplified in those cases of respiratory tract infection which are succeeded by renal and perinephric infection. For, while the nature of the first infection can generally be proved to be coccal, coliform infection is often all that can be definitely established bacteriologically for the second, so far as urinary findings go. Such are the cases which are so common in children and are generally called cases of pyelitis.

With regard to the urine: sometimes this is quite sterile, in spite of the presence of a suppurating focus in the cortex. Case 4 of my series is an example of this

Birdsall [8] in reporting sixteen cases of perinephric abscess found the urine normal in twelve. In some cases the staphylococcus is found over a certain period, when it is accompanied or replaced by the *Bacillus coli*. Such observations have offered the most certain proof of the secondary nature of the infection by the latter organism. Cabot and Nesbit [9] reported several cases in which these events occurred.

When we come to an examination of the pus taken from the kidney or perinephric tissue, the causal organism is more frequently identified and may offer a striking contrast with the bacteriological information obtained from the urine examination. Case 1 of my series is an example of such a case. Here *B. proteus* was obtained

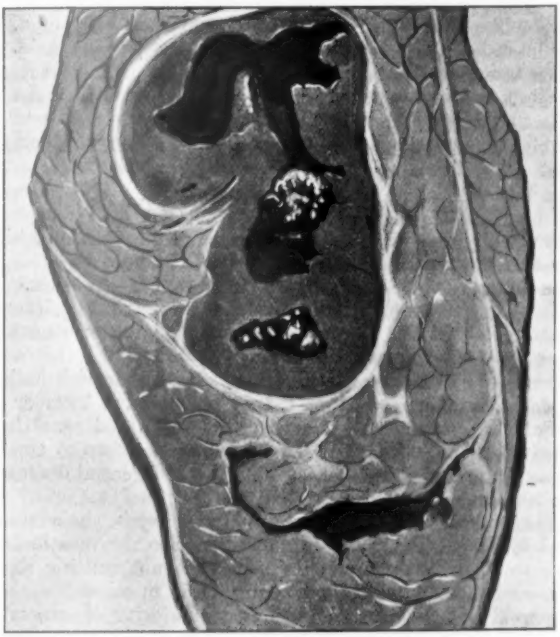


FIG. 1.—A left kidney containing stones, and its surrounding fat which was the seat of a perinephric abscess. Note the gross thickening of the true capsule. (Post-mortem specimen.) (Case 9.)

from the perinephric pus, while staphylococci and *B. coli* were revealed from the urine.

Judging by the reported cases the staphylococci are the chief offenders and these are most constant in connection with skin lesions. Richardson in 1915 [10] published a number of cases showing that the staphylococcus was the commonest organism in both the cortical and the perinephric abscess. Numerous reports which substantiate this view have followed. Joyce [11] reported seven cases of acute staphylococcal renal affection, confirmed at operation. In each case a peripheral lesion at a distance was identified as the source of the renal infection, and operation confirmed the presence of perinephric pus in all cases. Peacock, 1928 [12], in a study of twenty-one cases, showed that *Staphylococcus aureus* was present in pus from the abscesses in fifteen. Birdsall in sixteen cases of perinephric abscess

operated upon, reported *Staphylococcus aureus* present in the pus in nine, the others presenting other organisms. Blumenthal in his review of 1,500 cases from the literature, reported 90 % of cases due to staphylococcus.

Complications.—The most important of these occurs in the thorax. Pneumonia seems to be the commonest, with empyema and pleural effusion next. Pulmonary embolus also occurs, as Case 9 of my series shows.

The method of spread occurs in three different ways. First of all by ulceration directly through the diaphragm; Henry Morris described a case in which a large perinephric abscess had partly ulcerated through the diaphragm over an area the diameter of a penny-piece and opposite which the lung was adherent to the diaphragm. Another writer [13] reported the finding at autopsy of a perinephric abscess which had perforated the diaphragm and caused pneumonia and empyema. The efferents from the upper lateral lumbar lymphatic nodes pierce the crura of the diaphragm in passing upwards to join the thoracic duct. The embolism cases exemplify the spread of infection to the lungs by way of the blood-stream. In some cases in which it has been reported that perinephric abscess has followed pneumonia or other lung trouble, the question may quite well arise as to whether the perinephric abscess did not occur first.

Clinical Features and Diagnosis.

A careful study of numerous reported cases shows that a long history of illness previous to the correct diagnosis being made is not uncommon.

This at once indicates the difficulties which these cases present. Help is by no means always forthcoming from the discovery of the original source of infection, as this is often completely healed or never traced. A latent period before the renal complication sets in is the rule rather than the exception.

In the early stages of the disease the clinical features which indicate that there is an infection located in one or other kidney region have little or nothing about them which would enable one to exclude an uncomplicated renal infection as the cause. The fact that the ætiological factors which lead up to the two conditions are largely the same increases the task of making a differential diagnosis.

Perinephric abscess is sometimes only a terminal stage of pyelonephritis. Usually the majority of cases of the latter disease resolve in the course of a few days without clinical evidence that there is a perinephric extravasation of pus, so that it is when there are signs that the renal infection is not settling that the question of a perinephric complication will be kept continually in mind.

It is the general experience that the great majority of cases of perinephric abscess do not come to operation until an abnormal swelling is palpable in the loin. In some cases the delay is quite justifiable, because one knows that sometimes a kidney infection runs a somewhat protracted course and then finally settles. Personally, I have the conviction that operative treatment is called for, after only a short period of waiting. The case reports show that when this line of procedure has been followed, the early stages of perinephric extravasation are frequently encountered.

An especially difficult type of case is one showing constitutional, but no important localizing, signs of infection. There may be an absence of renal pain, tenderness or rigidity, or there may be insignificant urinary symptoms, and a urine entirely free from, or containing only scanty, pathological elements. Campbell, in reviewing eighty-three cases from the Bellevue Hospital, reported twenty-six, in which the diagnosis was only made at autopsy. And Barney [14], in reporting on 121 of coccus infection in and around the kidney, noted that in twenty-two cases found at autopsy there had been no clinical evidence of renal infection.

Small rises of temperature and only a slight degree of leucocytosis contrast strongly in some, with a considerable elevation of both in others. One must be

careful that these mild constitutional disturbances do not deter the investigator from a careful consideration of the upper urinary tract.

When carrying out a physical examination, it is important to make the patient sit up and lean forward, so that the loin may be inspected from behind. This procedure in well-marked cases will reveal a bulge in the lumbar region, where normally there should be a slight depression. On the other hand the alteration of contour may be so slight as to escape notice if the inspection is not made carefully. Another important physical sign to be made out on inspection is flexion of the thigh on the pelvis; hip-joint disease is easy to exclude by manipulating the limb. The appendix, however, must be thought of in these circumstances. Rigidity of the overlying abdominal muscles and tenderness in the same situation are prominent enough features in advanced cases, but in the early stages are unreliable signs, according to the variation in position of the initiating lesion in the kidney. At first these signs may be quite absent when the lesion is at or near the upper pole, in fact, the physical signs may point more strongly to the base of the corresponding lung, where dullness, diminished breathing, râles or crepitations may be noted, as a result of the adjacent inflammatory process just under the diaphragm.

The delayed onset of rigidity of the overlying anterior abdominal muscles applies also when the renal lesion is on the posterior aspect of the kidney. Again, an abscess on the anterior surface, near the lower pole, has more than once led to an unnecessary appendicectomy. One writer (Aschner) quoted three such instances from his series of sixty-one cases of staphylococcal infection of the renal parenchyma.

Frequency of micturition, dysuria, pyuria, hæmaturia or pain, tenderness or tumour in the loin, ultimately declare themselves in various combinations, and these at least focus interest on the urinary tract.

In a certain number of early cases the clinical features arouse suspicion, but do not convince. It requires a personal experience of the fact that an abscess may exist in the kidney, without any evidence in the urine of its presence, in order that one may be fully impressed that these circumstances can co-exist (Case 4).

When pyuria or hæmaturia occurs early, in combination with local renal signs, a full investigation will at least reveal the kidney as the source of the pus or blood.

Radiography has proved of the greatest possible assistance in diagnosing perinephric abscess. Plain skiagrams show the following features on the side of the infection: obliteration of the psoas outline and a scoliosis of the neighbouring spine, with the concavity towards the affected side (fig. 2).

Peacock reported ten out of eighteen of these cases with lateral curvature of the spine. These signs occur, however, in pyonephrosis without perinephric abscess.

In those difficult cases where the renal infection is seated at or in the vicinity of the upper pole, and in which the local physical signs are obscure, a plain skiagram and a screen examination may be of great assistance if the diaphragm can be seen to be pushed up and to be fixed or limited in its excursion on the side in question. Those who have had experience of stereoscopic radiographic investigation speak highly of it as a diagnostic measure. They claim that the kidney and ureter can be seen to be pushed anteriorly and sometimes laterally, and that the ureter curves like a bent bow.

An intravenous pyelogram (fig. 3) may show collections of the opaque medium in abscess cavities, both in the renal substance and in the perinephric region (Case 3). My experience with ascending pyelography has shown that a large perinephric abscess may be present, in spite of a normal pyelogram (Case 1). After all, this is quite in keeping with the known pathology, in which an abscess of the parenchyma is completely prevented by a fibrous tissue barrier from drainage into the calyces or pelvis. On the other hand, an ascending pyelogram may demonstrate in an unmistakable way the presence of an abscess cavity outside the kidney. This could

FIG. 2.—A plain skiagram showing obliteration of outer margin of psoas muscle and lowering of tip of 12th rib on the left side, which is the seat of a perinephric abscess. (Case 3.)

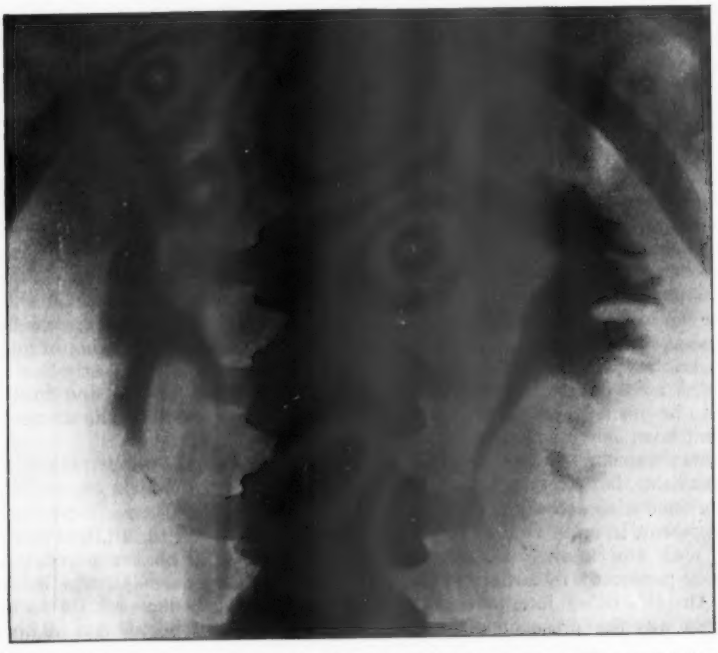


FIG. 3.—Intravenous pyelograms, showing two patches of opaque medium well below the lowest group of calyces on the left side, indicating abscess cavities. (Case 3.)

only occur when an abscess in the kidney discharged both into a calyx and into the perinephric region. Case 2 of my series presented a good example of this (figs. 4 and 5).

FIG. 4.—An ascending pyelogram which shows up a large abscess cavity outside the kidney. (Case 2)

TREATMENT AND PROGNOSIS.

From time to time one undoubtedly sees cases of perinephric infection accompanied by constitutional signs indicating suppuration, in which the symptoms subside without cutting down.

In the early stages there may be every reason to suspect the presence of pus, while it is impossible to know whether this is confined to the kidney or has extravasated externally.

The appearance of pus and blood in the urine may be regarded as an indication that the infective focus is draining by way of the natural channels of the kidney. Often this is sufficient to bring about resolution, and the symptoms subside (Case 2), but there may be also an extra renal accumulation which is not receiving adequate drainage and which may therefore require surgical aid. With this knowledge the case would be carefully watched. That a renal abscess can discharge itself both ways and heal without operation is clear from the case I have just reported.

In trying to come to a decision as to whether it is necessary to cut down, there is the knowledge, on the one hand, that a fairly prolonged pyrexia from a kidney

infection may suddenly settle without surgical interference, and on the other hand, that an exploration will most likely reveal a small amount of pus outside the kidney, that early operation gives better results than late, and that, even if there is no perinephric extravasation, a renal focus is almost certain to be found which could be drained with good results. My attitude is that one should explore early, when there

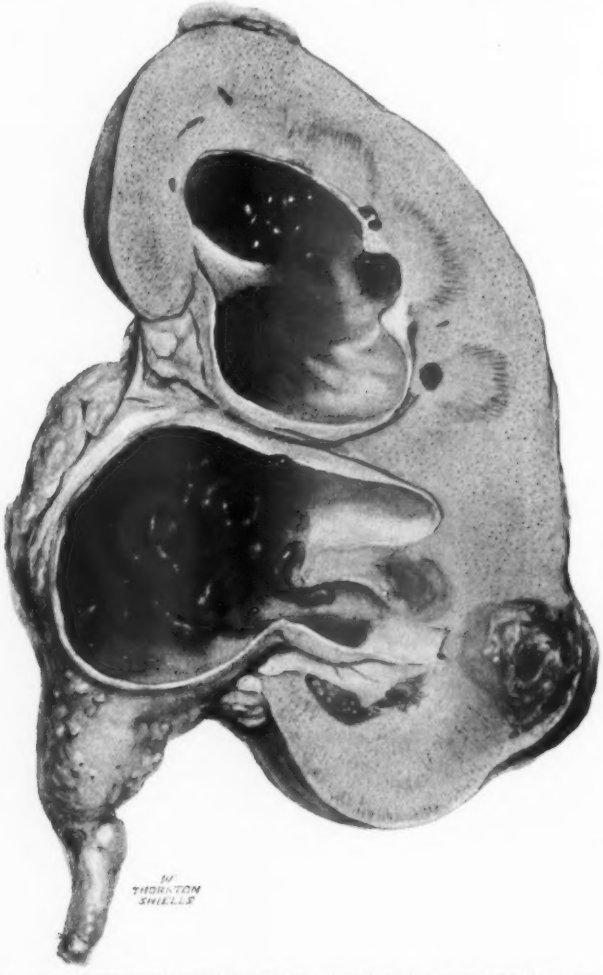


FIG. 5.—A hydronephrosis complicated by a localized inflammatory focus towards the lower pole and projecting from the outer border of the kidney. It is apparent that the area of infection which has given rise to the clots in the pelvis would most likely have resulted in a perinephric abscess had nephrectomy not been performed. (Case 11.)

is continued evidence of renal infection without pus or blood in the urine, and that one may wait longer when evidence is present that the abscess is draining by way of the renal pelvis.

The majority of perinephric abscess cases which come under the surgeon's notice are left until the local signs are advanced, often with bulging, and sometimes redness and œdema, of the loin. In the presence of a large perinephric abscess, the indication is obviously to evacuate the pus, while disturbing the kidney as little as possible. At the same time the finger not only explores for loculi in the perinephric tissue, but also explores the kidney itself. This may result in the evacuation of a focus of necrotic material from the renal substance. Case 4 of my series well illustrates the fact that the finger may successfully evacuate the renal focus without disturbing the kidney.

When the perinephric collection is small it may only be discovered while the kidney is being dissected free from its surroundings, while pus extravasated under —and still confined by—the true capsule, may escape notice unless decapsulation is carried out. On the other hand, a widespread disturbance of the kidney from its bed creates fresh dangers from a further distribution of the products of sepsis. Blumenthal, who collected data about 1,500 cases, reports that operators who limit themselves to the opening of the abscess give a mortality of from 4 to 14%, while those who expose the kidney for inspection give a mortality of from 18 to 25%.

Next we come to the important question as to the circumstances under which nephrectomy is advisable. In the presence of a large perinephric extravasation of pus, nephrectomy is against surgical principles. The disturbance of the protective barriers of fibrous tissue is likely to lead to infective complications. In those cases in which the perinephric infection has supervened on some chronic renal disease—such as stone, hydronephrosis or tuberculosis disease—nephrectomy will usually be necessary as a secondary measure at a later date, although in the last condition when the perinephric fluid is clear a primary nephrectomy is justifiable. (Case 6.)

When the perinephric abscess is small and it becomes obvious that there is an extensive area of necrosis in the kidney, the question of primary nephrectomy will receive more serious consideration. To extirpate the whole of the local focus of infection by nephrectomy would seem to offer good prospects of a satisfactory result. On the other hand, nephrectomy seems unnecessary when the renal focus can be enucleated with the finger, and this method gives good results.

To remove one kidney and to find later that the remaining organ has become the seat of infection which requires surgical interference is a possible eventuality which should always cause one to consider deeply before performing nephrectomy. Cases with this sequence of events have been reported. Again, where the original focus of infection is in connection with the lower urinary tract, as for example a prostatic abscess, there is a special danger of bilateral renal involvement.

Perinephric infection following trauma is a condition which, I think, requires separate mention, because from the beginning there is a perinephric extravasation of blood and sometimes of urine. In spite of this, in the great majority of cases the patients recover completely without operative interference.

Some years ago, before this Section,[1] I reported the results of treatment of forty-two cases of injury to the kidney; 73% of these were successfully treated by the non-operative method and none of these required subsequent operation. In a small proportion of cases in which expectant treatment is begun, evidence of perinephric infection determines surgical interference, after all—the indications for cutting down being persisting evidence of infection in the loin, and the increase in size of an existing swelling,

The results of delaying operation until perinephric infection is advanced are bad. In this type of case, however, drainage of the loin should be the first measure. It frequently happens that no later interference is necessary, but when there is

1 *Proceedings*, 1924, xvii (Sect. Urol.), 33.

secondary hæmorrhage to be dealt with, nephrectomy should not be delayed. The septic conditions under which the kidney is removed in these circumstances adds quite a considerable extra-operative risk. I have only once had to remove an injured kidney because of the onset of sepsis. (Case 5.)

CASES.

(1) *Right Perinephric Abscess following Pneumonia.*

E. M., female, aged 4. Three months after pneumonia, a large perinephric abscess was discovered on the right side. There had been abdominal pain for some weeks previously. Urine showed casts, red blood-cells, moderate number of pus cells, numerous staphylococci and some coliform bacilli. Right pyelogram showed no abnormality. Leucocytosis was 16,000. Operation: about 10 oz. of pus evacuated. Recovery. Pus yielded *B. proteus* on culture.

(2) *Right Perinephric Abscess following Tonsillitis.*

J. J., female, aged 8. Complained of painful and frequent micturition followed by a few drops of blood. Previously there had been frequent croupy cough and attacks of tonsillitis. Urine showed pus, pelvic and vesical cells, and many coliform bacilli. Cystoscopy revealed some recently bleeding ulcers about base of bladder. The right ureteric orifice was irregular in outline with redness and swelling. An ascending pyelogram of the right side showed a normal contour of the pelvis and calyces, together with a crescentic-shaped collection of opaque medium obviously lying outside of the lateral border of the kidney. On a closer inspection of the radiogram, one was able to make out that the tip of the ureteric catheter had passed beyond the highest limit of the uppermost calyx. The symptoms cleared up on expectant treatment and the urine became free from pathological elements (fig. 4).

(3) *Perinephric Abscess following Trauma and frequent Sore Throats.*

K. L., female, aged 12. Patient fell over while playing, and pain in the left side and hæmaturia followed on the same evening. Previously there were frequent sore throats. Evidence of infection in the left kidney region was noted. This persisted and hæmaturia continued. Later, slight bulging of the left loin posteriorly was noted. A plain skiagram showed an absence of the outer margin of the left psoas muscle and some scoliosis of the lumbar spine, with the concavity towards the affected side. An intravenous pyelogram showed a patch of opaque medium in the renal substance and another just outside the kidney border. These suggested intra- and extra-renal abscess cavities. My colleague, Mr. W. E. Tucker, who had asked me to see the case, cut down and found a small perinephric abscess surrounded by blood-clot (figs. 2 and 3).

(4) *Perinephric Abscess following Recurring Skin Disease.*

H. H., male, aged 18. Complained of pain in the left loin. History of recurring skin rash for years. Evidence of infection in the left kidney region gradually became established. No pathological elements found in the urine at several examinations. A plain skiagram showed obliteration of the outer margin of the left psoas muscle. A palpable swelling developed in the left loin. Operation. About half a pint of pus evacuated. A piece of renal tissue became dislodged. Intravenous pyelography subsequently showed a wedge-shaped deficiency on the outer border of the kidney. Recovery (fig. 6).

(5) *Perinephric Infection following Trauma to Kidney.*

Female, aged 20. The patient had fallen downstairs three days previously. The fall was followed by hæmaturia and signs of infection in the left kidney region. On examination, rigidity, tenderness, and resistance in left loin were noted. Temperature 103° F. Operation revealed a small amount of purulent fluid and blood-clot outside the kidney and a thin shell of renal tissue which had been separated from the whole of the anterior surface of the kidney. Nephrectomy. Recovery.

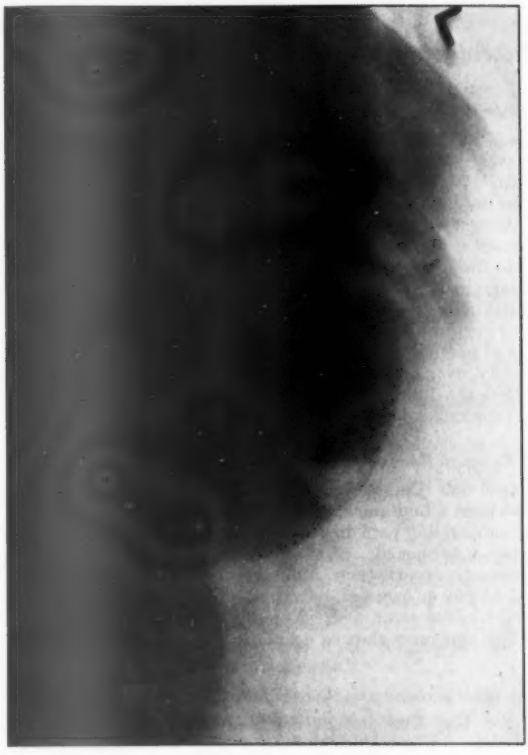


FIG. 6.—An intravenous pyelogram showing a triangular deficiency on the outer border of the left kidney in the lower half. From this gap a piece of necrosed renal tissue was dislodged during evacuation of a perinephric abscess. (Case 4.)

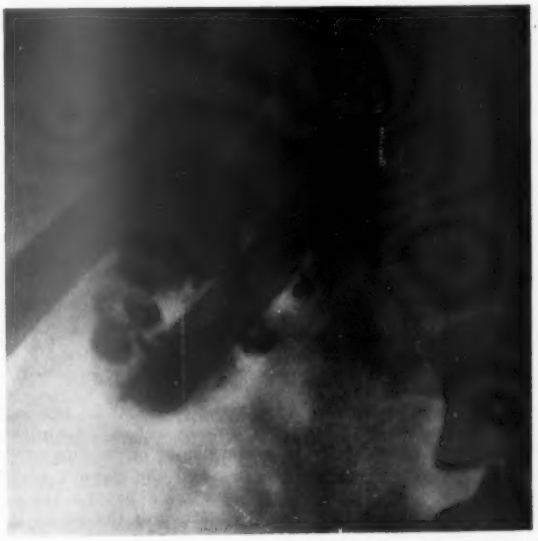


FIG. 7.—A plain radiogram showing masses of calcified tuberculous material in the right kidney This gave rise to a large perinephric cold abscess. (Case 6.)

(6) *Perinephric Abscess following Closed Renal Tuberculosis.*

P. G., male, aged 20. His only complaint was that he could see his right side to be swollen; he had never suffered discomfort in the renal region, nor had he any recollection of urinary symptoms. On examination, there was a typical perinephric bulging in the right lumbar region. The only pathological elements in the urine were a few pus cells detected microscopically. On cystoscopy one was able to make out that the right ureteric orifice was represented by no more than a slight depression which would not admit a ureteric catheter, while on the left side there were two ureteric orifices both functioning well, with effluxes of clear urine. A skiagram showed calcareous masses in the right renal region. Operation revealed a perinephric collection of clear yellowish fluid and a caseous and calcareous kidney. Nephrectomy was carried out, and a subsequent dissection of the kidney showed that it was without any vestige of parenchyma, while the attached half-inch of the ureter was shrunken and difficult to identify, even after careful dissection later. Microscopical examination of this structure showed that the lumen was completely obliterated by well-formed fibrous tissue with scattered muscle bundles towards the periphery (fig. 7).

(7) *Loin Sinus following Perinephric Abscess and Renal Tuberculosis.*

M. K., female, aged 42. Complained of a discharge from the left side. Nineteen years previously there had been albuminuria during pregnancy. Fourteen years later albuminuria was again noted accompanying pain in the left side. Three and a half years after this an abscess in the left loin was opened, and the sinus had been present for eighteen months when the patient came under my observation. A skiagram showed a calcareous mass in the left loin; the urine contained no pus or bacteria. Cystoscopy gave no evidence of function of the left kidney and a normal bladder was noted. Nephrectomy was carried out and the patient made a good recovery. The specimen showed a kidney which had been completely destroyed by tuberculosis.

(8) *Perinephric Abscess following Pyelolithotomy.*

G. D., male, aged 10. The patient complained of pain in both sides, vomiting and hæmaturia for two years. A skiagram showed a stone in each renal pelvis $\frac{1}{2}$ in. and $\frac{3}{4}$ in. in diameter respectively. Following left pyelolithotomy an abscess developed round upper half of left ureter. A skiagram showed obliteration of the outer border of the left psoas muscle and a slight scoliosis of the lumbar spine with its concavity to the left. Drainage. Recovery.

(9) *Perinephric Abscess following a Long History of Renal Calculi.*

E. C., female, aged 58. Stones had been removed from the left kidney twenty and eighteen years previously. The patient was admitted to hospital with a left perinephric abscess. A skiagram showed a number of stones in the left kidney. The abscess was opened and drained. The patient appeared to be doing well following the operation until the ninth day, when death occurred suddenly, from pulmonary embolus. Post-mortem examination of the left kidney showed old-standing perinephritis as well as recent infection (fig. 1).

(10) *Perinephric Abscess following a Long History of Renal Calculi.*

Miss W., aged 66. The patient passed several stones at the age of 8 and another stone at the age of 20. On admission to hospital a left perinephric abscess was present. This was opened and drained. A skiagram showed a mass of calculi bunched together in the left renal region. Nephrectomy was carried out several weeks after the drainage of the abscess. Recovery. The specimen showed a kidney atrophied to a length of two inches and containing many calculi.

(11) *Renal Abscess and Hydronephrosis.*

L. B., female, aged 60. The patient complained of blood in the urine for one week. Cystoscopy showed blood pouring from the right ureteric orifice. An intravenous pyelogram revealed a hydronephrosis on the right and a normal kidney on the left. Coliform bacilli were found in the urine. Nephrectomy was carried out and the patient made a good recovery. The specimen showed a large inflammatory focus bulging beyond the outer border of the kidney. Microscopy confirmed the inflammatory nature of the swelling (fig. 5).

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Discussion.—Dr. LANGDON BROWN said that in medical practice staphylococcic lesions and tonsillitis were of great importance in producing a perinephritis which, while falling short of suppuration, was associated with a true nephritis. When nephritis was accompanied by pain there was probably perinephritis as well, and in the absence of pyuria or skin lesions should suggest a critical examination of the tonsils as the most likely cause of the nephritis. With reference to trauma as a cause of perinephritis, he would instance the case of a boy who had hæmaturia after a kick over the right loin. His temperature rose to 103°, and he developed pyuria with *B. coli* in the urine. Before long, tubercle bacilli were found in the urine, and the boy died from tuberculous kidney with perinephritis. The trauma, presumably, had merely stirred up a latent tuberculous focus. In one case of *B. coli* pyelitis, the onset of perinephric abscess had been marked by complete suppression of the urine, which cleared up when the abscess was drained.

Mr. CLIFFORD MORSON said that he wished to stress the importance of conservative treatment in those cases of perinephritis in which the causal organism was the staphylococcus and the primary lesion existed in the skin as a boil. He strongly deprecated nephrectomy for what Israel was the first to call carbuncle of the kidney. No incision ought to be made into the perinephric tissues unless the surgeon was satisfied that pus was present. The condition was one of chronic septicæmia.

Mr. E. T. C. MILLIGAN: To avoid too sectional a conception of the causation of perinephric inflammation, it should be remembered that infection of any organ or structure behind the peritoneum can give rise to perinephric inflammation. Even an abscess behind the pelvic peritoneum can travel to the renal region. Furthermore, the appendix sometimes is a retro-peritoneal structure.

Loin tenderness is a common feature of acute pyelonephritis. If perinephric infection is common in pyelonephritis and is the cause of this loin tenderness, then the resolution of perinephric inflammation must be a common event, for perinephric abscess is admittedly a rare condition. In our experience, the resistance of retro-peritoneal fascia to infection after gunshot injuries and infected operations is not great, so that if peri-renal infection were the cause of loin tenderness in pyelonephritis, resolution would not be common and perinephric abscess would be seen more often.

In all but the stoutly built, bi-manual palpation in the loins will exclude tender peri-renal swelling caused by abscess formation, but where doubt exists in cases with unexplained high fever, the exploring needle should be freely and unhesitatingly employed. Information thus gained is more conclusive and reliable in cases of perinephric abscess than that obtained from skiagrams and pyelograms.

Inflammation has four terminations. (1) It has been suggested that resolution is perhaps more common than is supposed, in the peri-renal area. (2) Pus formation is the usual termination which calls for surgical interference. (3) Perinephritic gangrene, unlike the end result in pericolic inflammation, is very uncommon, because of the nature of the invading organisms. (4) When the perinephric inflammation ends in fibrosis, it accounts for the perinephric adhesions often found during operations on the kidney. In most cases these adhesions are easily separated, but this is not always so, and in two personal cases the kidney was so closely embedded in a mould of hard, almost cartilaginous tissue, that separation of planes of tissue, even subcapsular removal of the kidney, was impossible. Indeed this cement-like mass obscured the kidney and renal pedicle, obliterated all normal anatomical landmarks, and firmly bound all adjacent structures together in a hard fibrous mass. The kidney was functionless from blockage of the ureter in both cases. To cure an infected urinary loin sinus in one case, the kidney substance was removed piecemeal and the deep cavity remaining subsequently healed by second intention. In the second case the patient remains well and symptomless with his functionless embedded kidney.

Mr. H. L. ATTWATER said that perinephric suppuration was not a common disease. On the other hand, the milder forms of perinephric inflammation were most common, and in the course of operations on the kidney one encountered fibrous thickenings and adhesions in a large number of cases.

He had once operated in a case of a long-standing functionless painful kidney, seen in a pyelogram as about the size of a small hen's egg: this had been reduced to a small sac, and was embedded in dense fibro-fatty tissue, and was adherent in all directions; its removal was difficult. He, the speaker, had always wondered whether the long-standing perinephric inflammation had slowly compresssd the kidney and destroyed it, or whether the perinephric inflammation was secondary to long-standing disease of the kidney.

Mr. J. EVERIDGE: I was surprised to notice, in the series of cases quoted, the small percentage in which a cutaneous lesion had been the forerunner. In my experience this antecedent is far more common than Mr. Winsbury-White's figure of 1 in 10. There was quite an epidemic of such cases just after the late war, and the troops returning from the Middle East seemed peculiarly prone. I noted, too, that no mention was made of a perinephric suppuration secondary to retrocæcal appendicitis when pus had tracked in the retroperitoneal cellular tissue to the neighbourhood of the kidney. I have had several cases in which the differentiation from the usual type of perinephric abscess was extremely difficult, and only the odour of the pus at operation revealed the origin. Referring to abscess formation after pyelolithotomy, I think this complication can be avoided if prolonged and efficient drainage is adopted as a routine after this operation. It is our practice at King's College Hospital to drain for at least a week, and with this there appears to be little, if any, risk of abscess formation. I have not seen cases following an ascending infection from the genital adnexa, but have been on the look-out ever since the question was raised in this Section about five years ago—I think, by Mr. Nitch. We know that after urethral instrumentation severe renal pain may be felt, and organisms have been demonstrated in the capsular lymphatics when "catheter fever" has ended fatally. We should expect, therefore, to meet perinephric suppuration secondary to infection of the prostate and vesicles more commonly. Regarding diagnosis, and differential diagnosis from other more or less acute abdominal conditions: when organisms and pus are absent from the urine, and inflammation is entirely extraperitoneal, I have found that chromocystoscopy may be of assistance, the kidney compressed by the abscess being apparently less capable of excreting as much dye (indigo-carmine) as the healthy one; the comparison of urines withdrawn by ureteric catheters shows a marked difference in colour.

As to operation, I am definitely in favour of adopting the conservative line of treatment, namely, making an ample incision, evacuating the pus, and opening up loculi, remembering that the abscess may be widely spread around the kidney. With regard to the kidney itself, I am entirely against its dislocation and the too inquisitive investigation of it when it is surrounded by diffuse suppuration. In by far the greater number of cases the condition settles down well after this treatment, but the process of healing may be prolonged when there is an intra-renal focus.

Mr. WINSBURY-WHITE (in reply): Dr. Langdon Brown has referred to the pain of nephritis as being associated with perinephric changes. I fully agree that this is definitely evidence of some perinephric involvement. The pain in the kidney which is not due to some obstructive or other surgical condition is, I believe, mainly due to the inflammatory process which is spreading outwards from the true capsule of the kidney. The case of a tuberculous kidney in which the condition was unsuspected until the patient received an injury in that region, calls attention to the fact that surgical conditions may be present in a latent state as far as symptoms are concerned, and become stirred into activity by the injury—which may be extremely slight. Case 3 of my series falls into this category. The fact that hæmaturia and pain in the left side developed following a fall while the patient was running, strongly suggests that there was some pre-existing pathological condition of the kidney.

With regard to suppression of urine, this had not occurred as a symptom in any of the cases I have quoted.

Mr. Attwater has mentioned the frequent signs of perinephritis found on operating for surgical conditions of the kidney generally. This is a fact which has impressed me also, as I can recall no case of a diseased kidney upon which I have operated without finding perinephric reaction present in some degree.

Mr. Everidge has raised the point about the length of time that a drainage tube should be left in after an operation on the kidney for the removal of stone. I invariably continue the drainage by tube down to the side of the kidney incision, for one week, but in spite of this it is not uncommon to find a little tenderness down the line of the ureter. This is a feature which can quite easily be overlooked if one does not seek for it, as the patient, as a rule, does not complain of it. It is, however, unusual for this sign of infection down the ureter to lead to anything more unpleasant. Since my experience with the case which I have reported this evening, I have made the rule of placing a piece of rubber tissue for drainage purposes alongside the upper portion of the ureter.

The obliteration of the psoas margin, to which reference has been made as being a diagnostic sign of perinephric abscess, is seen also in some cases of hydronephrosis. One must therefore be careful in interpreting a radiogram which has this feature.

JOINT DISCUSSION No. 6.

Section of Tropical Diseases and Parasitology and Section of Medicine.

Chairman—Dr. J. GORDON THOMSON (President of the Section of Tropical Diseases and Parasitology).

[*April* 7, 1932.]

DISCUSSION ON THE MEGALOCYTIC ANÆMIAS OF TROPICAL AND NON-TROPICAL COUNTRIES.

Dr. L. J. Witts: Our subject to-night is of practical importance as well as of theoretical interest. The terms "pernicious anæmia" and "megalocytic anæmia" have often been used as if they were interchangeable, but they are by no means synonymous. It is fortunate that pernicious and allied anæmias account for the great majority of megalocytic anæmias—fortunate, because they respond well to treatment. Nevertheless, there remains a residue of cases of megalocytic anæmia which are of quite different ætiology, which may tax our powers of diagnosis to the utmost, and which are often sadly resistant to treatment.

When we speak of the size of the red cells we may be referring either to their volume or their diameter. It will simplify our discussion if we confine it to the diameter, as in this way we shall exclude acholuric familial jaundice, in which the cells are constitutionally of an abnormal, spherical shape, and have a smaller diameter but a higher volume than normal. Price Jones has constructed a frequency distribution curve which embraces all the possible variations in diameter of healthy erythrocytes. Cells which fall to the right of the normal curve are megalocytes, and a megalocytic anæmia is one in which such cells are present. The curve of the distribution of red-cell diameters gives much more information than the mean diameter of the cells, for megalocytes are always pathological, whatever the mean diameter. We may make the crude generalization, which is perhaps not free from exceptions, that the appearance of megalocytes in the peripheral blood connotes the proliferation of megaloblasts in the bone-marrow.

Megaloblasts proliferate in the bone-marrow under two very different sets of circumstances. The first is the megaloblastic degeneration of the bone-marrow which occurs in Addison's anæmia and a variety of related anæmias. The second is the multiplication of megaloblasts when blood-formation is greatly accelerated, as happens at times in the hæmolytic anæmias. The megaloblastic degeneration of the bone-marrow in Addison's anæmia and allied states is attended by a diminished output of cells from the marrow, and I have recently suggested that these diseases in which hyperplasia of the bone-marrow accompanies a diminished formation of blood may be grouped together under the title of "anhæmopoietic anæmias" [17].

The Anhæmopoietic Anæmias.

The group of anhæmopoietic anæmias includes the majority of the idiopathic anæmias and a high percentage of the megalocytic anæmias. We consider these anhæmopoietic anæmias to be due to a disturbance in the normal development and delivery into the circulation of the red cells. In health the cells develop smoothly from the primitive reticulo-endothelium, through megaloblast and normoblast, to erythrocyte, and few megaloblasts or none can be recognized in the marrow. When

the nutrition of the blood-forming organs is disturbed, either from defective diet or from the failure of digestion and assimilation in the alimentary canal, the orderly ripening of the red cells may be disorganized and the process may be arrested at one or other of these levels. In iron deficiency, for example, there is normoblastic degeneration of the bone-marrow and a microcytic anæmia. Vitamin B deficiency may be attended by megaloblastic degeneration of the bone-marrow and a megalocytic anæmia. In extreme malnutrition, such as occurs in late sprue, erythropoiesis ceases entirely and there is aplastic anæmia. "The anæmia is due to diminished blood-formation or anhæmopoiesis, and according to the level at which hæmopoiesis is arrested, the marrow may be normoblastic, megaloblastic or aplastic. The cells drafted into the circulation from this dysplastic marrow are sometimes abnormal and liable to early destruction, but hæmolysis is always secondary to the degeneration of the bone-marrow and is never of high degree. The reticulocyte count is low, the resistance to hypotonic saline is little impaired, and hæmoglobinuria and hæmoglobinæmia never occur. The white cells and the platelets are normal or diminished. Remission of the disease is attended by an outpouring of reticulocytes in numbers directly proportional to the extent of the hyperplasia of the bone-marrow. All these features are in direct contrast to the hæmolytic anæmias, which will be described later. Clinically, these anæmias are characterized by their frequent association with glossitis, gastro-intestinal disorders and degeneration of the nervous system" [17]. To-day we are concerned only with such of the anhæmopoietic anæmias as are of a megalocytic type, but these form a sufficiently imposing group.

I shall not enter on a detailed description of the anhæmopoietic megalocytic anæmias, as other speakers are more familiar with those of tropical origin, while I have discussed the non-tropical varieties on a recent occasion. Megalocytic anæmia from errors of diet is uncommon in the temperate zones, though it may occur in the more fanatical type of vegetarian and it responds to treatment by liver [8]. The non-tropical megalocytic anæmias are usually due to disorders of the gastro-intestinal tract and Addison's anæmia is of course the most important example. We now attribute Addison's anæmia to the achylia which is its most constant symptom. In normal gastric digestion a principle is elaborated from the proteins of the food which ensures the orderly maturation of megaloblasts with normoblasts and satisfactory erythropoiesis. We might define pernicious anæmia as anæmia due to lack of the hæmatinic principle which is normally elaborated by the action of the proteolytic ferments of the stomach, absorbed from the intestine and stored in the liver and to a less extent in other organs. Such a definition would prepare us for the recognition of identical megalocytic anæmia when the intestine is diseased. Of such an event the most important examples are: (1) Intestinal anæmia, such as occurs, (i) after resection of the small intestine, (ii) in intestinal stenosis, (iii) when the intestine is infested with parasites such as *Dibothriocephalus latus*, and (iv) in certain cases of chronic ulceration of the bowel.

(2) The anæmias of fatty diarrhœa, which occur in cœliac disease, sprue, chylous diarrhœa, pancreatic diarrhœa and gastro-colic fistula.

Let me make it quite clear that the anæmia of these diseases is not always of the megalocytic type. It may be aplastic or normoblastic. Nevertheless megalocytic anæmia occurs frequently in each and all and responds to treatment by liver. We are still uncertain how far these anæmias are due to diminished absorption of the hæmatinic principles from the intestine and how far they are due to impaired gastric digestion, for evidence of gastric disease, more especially deficient proteolytic activity of the stomach, is present in a high proportion of cases of intestinal disease. We have reliable evidence that the stomach is perfectly normal in some of these cases [1], and in such cases it remains to decide whether the anæmia is due to failure to assimilate the liver principle (which is effective in Addison's anæmia), or the vitamin B complex (which is effective in tropical macrocytic anæmia but not in Addison's anæmia) or perhaps other unknown factors.

Acute Hæmolytic Anæmia.

The second set of circumstances which may give rise to megalocytic anæmia is an acceleration of the process of blood destruction. The megalocytic anæmias of hæmolytic origin may be subdivided according as they are acute (when they are probably due to infection), or chronic (when they often seem to be the result of some primary disease of the liver, spleen or blood-forming organs). The typical response to infection is of course a secondary anæmia in which the cells are below the normal size. A high colour-index may be present when large numbers of red cells are suddenly destroyed by chemical or bacterial toxins, and also immediately after a hæmorrhage, but it is the rarest event for a true megalocytic anæmia to develop under those circumstances. During recovery from the hæmolysis or hæmorrhage megaloblasts may be swept into the circulating blood but the colour-index falls and the red cells become smaller than normal. The infectious anæmias in which

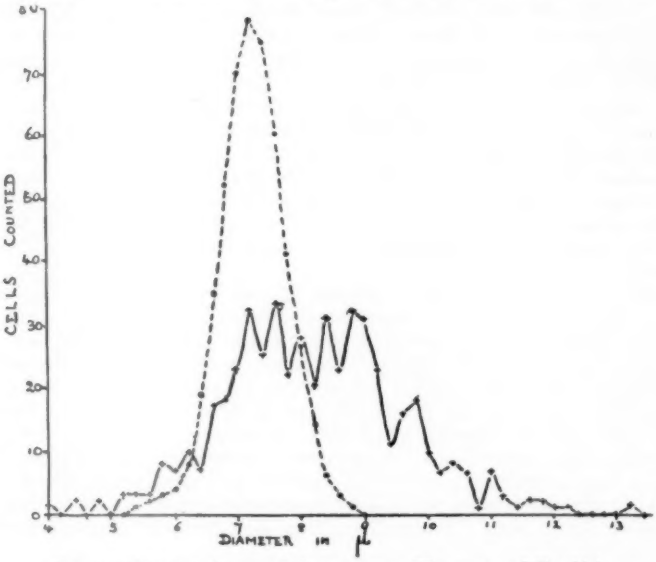

FIG. 1.—Megalocytic anæmia in pregnancy (Hampson and Shackle).

megalocytosis has been demonstrated are of a subacute or chronic type, for it is only when blood destruction is increased for a period of some time that the level of differentiation and development of red cells is at all likely to be shifted back to the megaloblastic-megalocytic stage. At any rate, megalocytosis is a very uncommon type of response to infection, though it has been described in Bartonella infection [10] and rare cases of malaria [3]. In the acute hæmolytic anæmias of unknown origin, of the type described by Lederer and Brill, the character of the anæmia is not constant. The cells were normal or smaller than normal, in spite of a high colour-index, in three cases of this type in which Price Jones curves were made at Guy's Hospital [11], but Christiansen reports a case with a mean red-cell diameter of 8·01 m. In the grave hæmolytic anæmias of pregnancy, the size of the red cells varies from case to case, but there may be frank megalocytosis as is shown by the Price Jones curves published by Hampson and Shackle (fig. 1) and by Parvu and Fouquiau. Recent observations [16, 18] suggest that megalocytic anæmia in

pregnancy is a true pernicious anæmia due to gastric disease, and that it is therefore anhæmopoietic and not hæmolytic in type; it is probable that the acute hæmolytic anæmia of Lederer also occurs in the pregnant woman, but reliable information on this point and detailed blood-pictures are still lacking. The treatment of the acute hæmolytic anæmias is that of the primary infection, when it is known; in the idiopathic cases transfusion is often dramatically successful; liver also seems to be of value.

Chronic Hæmolytic Anæmia.

Within the last few years, largely as a result of the work of P. N. Panton, L. S. P. Davidson and G. W. Goodhart in this country, we have come to recognize a group of cases in which the clinical picture is that of a chronic hæmolytic anæmia of a fairly constant type, though the ætiology and pathology of individual cases may be quite different. They are important clinically, as they are easily confused with pernicious anæmia and with acholuric jaundice, though careful study of the history and the blood-picture should always serve to differentiate them. They differ from pernicious anæmia in the absence of involvement of the gastro-intestinal tract or the central nervous system, and in the presence of continuous excessive hæmolysis, as shown by persistent high reticulocytosis and crises of blood destruction in which free hæmoglobin may appear in the plasma and the urine. The fragility of the red cells may be increased. They differ from acholuric jaundice in the absence of any hereditary element and in the fact that the red cells are of normal shape and frequently of high diameter. In some of these cases the syndrome is grafted on to a well-known primary disease, in other cases it appears to arise as an independent entity. The mechanism underlying the hæmolysis in these cases is still unelucidated.

Leukæmia.—The association of anæmia of high colour-index with leukæmia of an acute or aleukæmic type, has been known for many years. In 1920 Wanner published an extremely able review of these cases, and the subject was recently brought up to date by Reichel (1930). The anæmia is often of the utmost severity and normoblasts and megaloblasts appear in the peripheral blood. I have no knowledge of the behaviour of the reticulocytes in these patients, but polychromasia is marked and van den Bergh's reaction is positive. At autopsy there may be hæmosiderosis of the liver, spleen, kidneys, and bone-marrow, and megaloblasts may be present in large numbers in the bone-marrow, in the midst of the proliferating white cells. I am fortunate in being able to reproduce a Price Jones curve made from one of these cases at Guy's Hospital by Hampson and Shackle. It shows frank megalocytosis (fig. 2).

Lymphadenoma.—The anæmia of Hodgkin's disease is usually of the aplastic or hypoplastic type, and the size of the red cells is diminished. The anæmia runs parallel to the course of the disease, and in the remissions there may be a reticulocyte crisis as the blood improves. In rare instances, of which L. S. P. Davidson has reported four examples, the blood picture is entirely different. The patient presents himself with a chronic hæmolytic anæmia, the red-cell count may be below a million, the colour-index is above unity, and megaloblasts appear in the peripheral blood. Reticulocyte counts of from 10% to 50% may be present for long periods. The Price Jones curve may show gross megalocytosis. The diagnosis of these cases offers the greatest difficulty, as the early symptoms may be not at all typical of Hodgkin's disease and enlargement of glands may be a late event.

Splenic anæmia.—I have recently seen a case of the same type, a report of which is shortly to be published by Professor Robert Donaldson and myself, in which a chronic hæmolytic anæmia with persistent high reticulocytosis and fluctuating jaundice followed pregnancy. The woman died after an illness of two years, and at autopsy we found a greatly enlarged and congested spleen in association with a liver which showed early portal cirrhosis. The anæmia was of the microcytic

type throughout and the colour-index was below unity, although an abnormal number of megaloblasts were present in the marrow. In its other features the case corresponded so closely with the hæmolytic anæmias of leukæmia, lymphadenoma and the idiopathic type, that we may expect to find occasional cases of splenic anæmia with a hæmolytic, megalocytic anæmia.

Idiopathic cases.—Finally there are the idiopathic cases of chronic hæmolytic anæmia of this type, in which the only abnormal signs after death are hæmosiderosis of the viscera and great hyperplasia of the bone-marrow. The symptoms are purely and simply those of a chronic and long-sustained hæmolysis which terminates in death from anæmia and exhaustion. Hæmosiderosis is not necessarily confined to the viscera, for iron pigment may be deposited in the skin or excreted in the urine.

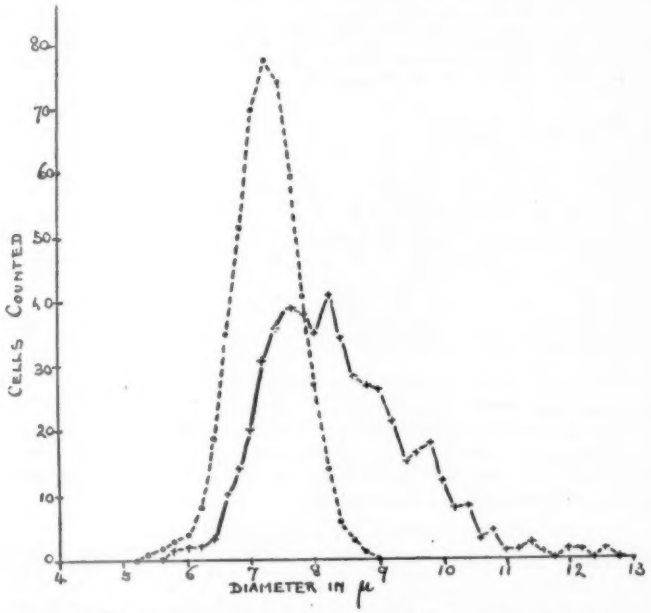

FIG. 2.—Megalocytosis in aleukæmic leukæmia (Hampson and Shackle).

Obscure though these anæmias are, it seems probable that a common factor underlies them all. They are usually, but by no means always, of a megalocytic type. The degree of anisocytosis is rarely high, and the effect is as if the curve of distribution of the red-cell diameters were shifted bodily to the right. All this suggests that they are due to a morbid exaggeration of the hæmolytic activities of the organism, rather than to any primary disturbance of the red cells or the erythropoietic tissues. Treatment is difficult, and in the present state of knowledge no hope can be offered in the cases which are based on leukæmia or lymphadenoma. Liver is useless and transfusion often harmful. When the spleen is enlarged, benefit may follow its removal, but the issue of the operation is always doubtful and impossible to predict.

It is possible to make only a rough estimate of the frequency of the different types of megalocytic anæmia. In my experience Addison's anæmia, and similar anhæmopoietic anæmias due to disturbances of nutrition or digestion, account for from 90%

to 95% of all the megalocytic anæmias in this country. Chronic hæmolytic anæmia is responsible for some 5%, and acute hæmolytic anæmia for only from 1% to 2%. In hospital and consultant practice we see patients who have not done well on treatment with liver, and among these the percentage of megalocytic anæmias of a non-Addisonian type is higher.

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Dr. N. Hamilton Fairley:—

Megalocytic Anæmia in the Tropics, with Special Reference to Sprue.[1]

The various megalocytic anæmias met with in Europe have a world-wide distribution, while in addition there are certain diseases peculiar to warm climates which produce a blood-picture indistinguishable from that of pernicious anæmia. The tropical practitioner, therefore, has to be familiar with all varieties if his diagnosis is to be efficient and his therapeutics effective.

A megalocytic anæmia may be defined as one characterized by an excessive number of megalocytes in the peripheral blood, leading, as a rule, to a demonstrable increase in the average diameter of the red cell. A considerable degree of anisocytosis is characteristic, and the Price Jones curves, apart from asymmetry and displacement to the right, generally show a broadening of the base, extending in both directions. These anæmias are always associated with a variable degree of megaloblastic reaction in the bone-marrow, and those of alimentary origin, at least, respond specifically to the administration of adequate quantities of liver extract or marmite, with a reticulocytosis and rapid blood regeneration.

I.—Hæmolytic Origin of Megalocytic Anæmias.

Bunting (1905) and others, many years ago showed experimentally in rabbits subjected to intravenous injections of small doses of hæmolytic chemicals like ricin and saponin, that marrow injury, followed by a megaloblastic hypertrophy, occurred, associated with an excess of megalocytes and the appearance of megaloblasts in the peripheral blood. These experiments made it possible to understand why a hæmolytic anæmia might present a megalocytic blood-picture. Until recently hæmosiderosis and hyperbilirubinæmia had been accepted as valid evidence of excessive blood-destruction, and many authorities had come to regard pernicious anæmia as itself of hæmolytic origin. Such views, however, have lost caste and are no longer tenable. As a matter of fact, hæmolytic anæmia almost invariably induces an erythroblastic response in the bone-marrow and in consequence is associated with an anæmia of a microcytic or normocytic type. Malaria is a typical hæmolytic anæmia, and though one meets severe grade malarial anæmias which in many respects clinically resemble pernicious anæmia, none in my experience have ever conformed to the hæmatological criteria justifying such a diagnosis.

Carrion's disease (*Oroya fever and verruga peruana*).—The only tropical megalo-

[1] I have to acknowledge my indebtedness to the Colonial Medical Research Council for supplying the services of Mr. R. J. Bromfield as biochemical assistant during the investigation under review.

cytic anæmia which can claim a hæmolytic origin appears to be Oroya fever, caused by *Bartonella bacilliformis* located in the red cells. This disease, which is limited to towns on the west side of the Andes, is characterized clinically by initial malaise and apathy, followed by irregular remittent fever, cephalalgia, and pains in the bones and joints. Tenderness over the sternum, hæmolytic jaundice, albuminuria, petechial hæmorrhage, splenomegaly, enlargement of the lymph glands, and a rapidly developing pernicious anæmia complete the picture. Not infrequently red-cell counts of less than 1,000,000 per c.mm. develop within a few days. The colour-index exceeds 1·0, and blood-smears show poikilocytosis, anisocytosis, polychromatophilia, normoblasts and megaloblasts which, in fulminating cases, may be numerous. There is generally a leucocytosis of about 20,000 per c.mm. and the differential count shows from 60% to 70% of neutrophiles; immature neutrophil granulocytes, metamyelocytes, and even myelocytes, are said to be common. Monge and Weiss (1927) state that the Arneth index shows a shift to the left. From a hæmatological viewpoint the Bartonella anæmias are of great interest, owing to the rapidity with which megaloblastic hypertrophy of the red marrow must ensue. The degree of blood-destruction is very severe, and it is interesting to note in that most fatal of all hæmolytic anæmias, blackwater fever—in which hæmolytic jaundice, hæmoglobinæmia, and hæmoglobinuria rapidly occur—that erythroblastic hypertrophy of the red marrow invariably follows and the anæmia is never megalocytic in type. Noguchi's (1927) work confirms the view of the older Peruvian physicians that Oroya fever is really the febrile stage of "verruga peruana," the cutaneous lesions of which develop later. Only especially susceptible individuals infected with *B. bacilliformis* appear to develop Oroya fever, and it may be that, just as splenectomy or deficient dietary is necessary to induce Bartonella anæmia in latently infected rats, so in man some other factor may be necessary to precipitate the generalized septicæmia and acute hæmolytic anæmia which characterize the febrile stage of this disease.

II.—Megalocytic Anæmias of Nutritional and Alimentary Origin.

Whipple (1920) and his colleagues, working on experimentally induced anæmias in dogs, first proved the fundamental importance of different dietaries in blood-restoration, and it was during the clinical applications of this knowledge to man that Minot and Murphy (1926) made their remarkable discovery regarding the unique therapeutic value of whole liver in pernicious anæmia. Recently Castle (1929) has shown that there is some "intrinsic factor" (proteolytic enzyme) secreted by the normal stomach which, acting on protein, produces a hæmatinic substance necessary for the normal functioning of the red marrow, and that in its absence megaloblastic hypertrophy ensues, with the production of megalocytic anæmia; furthermore, in cases of pernicious anæmia, sprue, and intestinal fistulæ, he has demonstrated that the stomach fails to produce this proteolytic enzyme. This new knowledge has shed much light on the alimentary origin of many obscure anæmias, and it is now evident that the defective production of Castle's "intrinsic factor" in the stomach, or its destruction or mal-absorption in the small intestine, would result in megalocytic anæmia. The nutritional origin of the tropical megalocytic anæmia, especially in its relationship to pregnancy, is being dealt with in detail by Dr. Wills, and I will confine my subsequent remarks mainly to dibothriocephalus anæmia and tropical sprue, especially comparing and contrasting this disease with pernicious anæmia.

Dibothriocephalus anæmia.—Of the megalocytic anæmias originating in the small intestine that of the broad tape-worm—*Dibothriocephalus latus*—is perhaps the most difficult to understand. Indistinguishable in its hæmatological aspects from pernicious anæmia, Erstrom (1927) has shown that in Finland it occurs in only from 1 to 5 per thousand of infected persons, so that some other factor, such as a constitutional predisposition, appears to be necessary for its development. Many cases show achlorhydria, but in certain of these, as in the patient reported by Mills (1931), acid

secretion reappears after elimination of the parasites. Liver extract produces a typical reticulocytosis and restores the blood-count to a normal level, but relapses recur later unless effective anthelminthic remedies have been instituted. In severely anæmic patients specific treatment may be contra-indicated until liver extract therapy has resulted in improvement. Cases have been recorded which relapsed years after the worms had been entirely expelled, and similarly I have noted in cases of sprue which have been apparently cured over considerable periods of time, that megalocytic anæmia may recur in the entire absence of intestinal symptoms. Attention has already been drawn to the high incidence of achlorhydria in people harbouring *Dibothriocephalus latus* and possibly the secretion of Castle's "intrinsic factor" may similarly be affected, thus affording a gastrogenous basis for the anæmia. Or again, after it has been produced, the hæmatinic substance may be destroyed or poorly absorbed in the small intestine of the host, as a result of toxic effects exerted by this parasite. Obviously the gastro-intestinal derangement which ensues has not a mechanical or reflex origin, for otherwise similar anæmias would be encountered in infestation with *T. saginata* and *T. solium*.

Tropical Sprue.

The anæmia of tropical sprue closely resembles that of pernicious anæmia and there is still a good deal of confusion regarding the duality of these two diseases. Sprue itself is a gastro-intestinal malady, characterized clinically by morning diarrhœa, abdominal flatulence, marked loss of weight, sore tongue and buccal apthæ, anæmia, asthenia, low blood-pressure, and a dry and sometimes pigmented skin, which however rarely shows the yellow appearance seen in pernicious anæmia; furthermore, the loss of weight is far greater in sprue, and neurological features are absent. Typically the stools are pale, bulky, and frothy, acid to litmus, and containing an excess of fat which is adequately split. Cramps and tetany occasionally complicate the picture. At autopsy there is typically an entire absence of yellow subcutaneous fat, the heart is small, and the small intestine atrophied, the bowel wall often presenting a diaphanous, parchment-like appearance. In all these respects the post-mortem findings differ from those of pernicious anæmia. The bone-marrow in the two diseases sometimes presents an identical appearance, but generally, in sprue, megaloblastic tissue fails to fill the long bones completely, being interspersed between areas of yellow marrow or the greenish-yellow gelatinous marrow met with in certain nutritional diseases.

Blood-counts in sprue.—The degree of anæmia varies at different stages of the disease and during the first few months may be entirely absent. In eleven out of sixteen instances in Bombay, in which the patient had been ill for less than three months, Fairley, Mackie, and Billimoria (1929) found that the red-cell counts were normal and the hæmoglobin values only slightly reduced. In subsequent relapses anæmia is a more constant feature of the disease, and in a recent series of 62 cases examined at the Hospital for Tropical Diseases, London, the average count of red blood-cells was 2,933,000 per c.mm., the hæmoglobin 59 %, and the colour index = 1·0. In pernicious anæmia, Cabot (1927) has pointed out that from 84% to 89 % of cases have counts under 2,000,000 per c.mm. at the first examination. This strikingly illustrates one of the fundamental clinical differences in the onset of the two diseases, for patients with sprue seek medical advice for intestinal trouble and rarely, if ever, on account of anæmia. In cases of relapsing sprue, however, especially those following a respiratory infection in the winter months, anæmia may initiate a relapse.

The blood-picture in sprue.—The blood-picture in the average case of sprue is one of mild megalocytic anæmia, poikilocytosis, and anisocytosis being present and sometimes polychromasia, while an increase in the megalocytes is generally evident. As a rule, however, the changes are not nearly so striking as in pernicious anæmia,

an obvious explanation being that the anæmia itself is not of the same severity. In the group of sprue cases with counts under 2,000,000 corpuscles per c.mm., in addition to the changes mentioned above, one meets with basophilic stippling and an occasional normoblast or even megaloblast. Nucleated red cells, however, are not as common as in pernicious anæmia, the reason probably being that, as a rule, there is not so much megaloblastic tissue in the bone-marrow of sprue cases.

In the literature there are frequent references to aplastic anæmia in sprue, but a true aplastic blood-picture is rarely found in this disease in England. Occasional cases of this type were met with in the Bombay series, and one woman with recurrent sprue went downhill progressively after her second relapse, without any significant increase in the bilirubin content of the plasma or the appearance of regenerative forms in the peripheral blood, finally dying from profound anæmia.

The diameter of the corpuscles in sprue. (1) Price Jones curves.—Hampson and Shackle (1924) described Price Jones curves in three cases of sprue, and found marked displacement to the right. The mean diameters of the corpuscles were 8·3, 8·87, and 9·0 microns, and in their cases a typical megalocytic anæmia was demonstrated. Fairley, Mackie, and Billimoria (1929) confirmed these findings in 11 cases of sprue, 10 of which presented Price Jones curves resembling those met with in pernicious anæmia: the average red-cell diameter for the series equalled 8·0 microns. In only one case was the apex of the curve displaced to the left of the normal, and here the mean diameter, which was 7·11 microns, fell within normal limits. This case proved of exceptional interest, for four months later the patient returned to hospital with a most profound anæmia; the corpuscles then equalled 400,000 per c.mm., the hæmoglobin 10 %, and the colour-index 1·2. At autopsy the tibia was filled with megaloblastic marrow identical with that observed in pernicious anæmia.

In the London series in only two cases were Price Jones curves investigated—and, in both, by Price Jones himself. Both presented pictures of pernicious anæmia as regards the red cells. The mean diameter in one case (7·6 microns) fell within normal limits, but the coefficient of variation was over 12 %. Following liver therapy both cases responded with an intense reticulocytosis, and blood restoration to a normal level ensued. Early in the disease hæmoglobin may sometimes be slightly decreased and a mild degree of secondary anæmia may be encountered, but in the absence of complications a well-established sprue anæmia is almost invariably megalocytic in type, and the Price Jones curve as well as halometer measurement show this to be so, even when the colour-index is definitely under 1·0.

(2) Diffraction micrometry.—This method, though not so informative or so accurate as the Price Jones curve, has afforded information of value in routine work. In a consecutive series of 58 cases of sprue investigated by Eve's halometer, seven showed an average corpuscular diameter of 7·6 microns or less, 12 of 7·8 microns or less, while in 39 cases the readings varied between 8·0 and 8·6 microns. As readings of 7·8 microns in non-megalocytic anæmias may occasionally be encountered, I have only accepted readings of 8·0 microns or higher as indicating an anæmia of megalocytic type, and adopting this standard, 39 cases would be classified as megalocytic, 12 as doubtful and 7 as normal. Of the latter group the blood-counts were normal in 3, while 4 presented only a mild degree of anæmia with a colour-index not exceeding unity. Apart from any assistance which diffraction micrometry may afford in routine diagnosis, the method subserves a useful purpose in indicating a decrease in the average size of the corpuscle, under treatment.

Response to liver extract therapy.—In the treatment of sprue it is essential to control intestinal features—such as flatulence, abdominal distension, and diarrhœa—by rest in bed and suitable dietary, and provided this is accomplished, liver extract therapy clears up the megalocytic anæmia of sprue as effectively as it does

pernicious anæmia. Thus, in a recent series of 33 cases treated with high meat protein diet and liver extract (= 1 to 1½ lb. daily), the average gain in corpuscles = 1,660,000 per c.mm. and in hæmoglobin = 20%, while in another series of cases given a high milk protein diet (Sprulac) [1] the corpuscles increased by 1,926,000 per c.mm. and the hæmoglobin by 20%. The maximal reticulocytosis in the two series averaged 15·9 and 17·1 per cent. respectively. Paralleling the improvement in the blood-counts, there was a decrease in the colour-index and the average diameter of the corpuscles. Once the blood-counts and the average diameter of the corpuscle have reached the normal, a maintenance dose of liver extract does not appear necessary in most cases of sprue, though it is probably safer to advise a continuation of liver extract (= ½ lb. daily) for three months after apparent recovery. Hepatex (P.A.F.) administered intravenously or intramuscularly has been found of value in reinforcing liver extract *per os*, but given alone it does not appear to initiate the early reticulocytosis and sustained blood-response reported in pernicious anæmia. In a case of sprue recently reported by Rogers and Cooke (1932), liver extract proved ineffective until combined with intravenous injections of hepatex (P.A.F.) and large doses of iron *per os*.

The fractional test meal.—The fractional test meal often affords information of value in differentiating sprue from pernicious anæmia, for though nearly 60% of sprue cases show hypochlorhydria or actual achlorhydria, free hydrochloric acid is demonstrable in at least 70% of cases if histamine (¼ mg.) be injected. Furthermore, even in cases not responding to histamine, pepsin and rennin may sometimes persist in the gastric juice. I have observed patients with hyperchlorhydria who, on acquiring sprue, have passed through a stage of hypochlorhydria to one of achlorhydria, with loss of response to histamine, and after recovery have reverted to the original hyperacid curve. Undoubtedly, with recovery, normal acid secretion gradually tends to be re-established in many of the achlorhydria cases. Probably exceptions do occur when an acquired achylia gastrica becomes permanently established, and it is in such cases that megalocytic anæmia may result years after the disappearance of all sprue symptoms. One such case recently came to autopsy, and the pathological findings were those of pernicious anæmia. Megaloblastic marrow filled the long bones, the heart was enlarged and fatty, the intestine was normal, and a thick layer of bright yellow subcutaneous fat covered the body.

Bilirubin content of the blood in sprue.—The van den Bergh test invariably yields a negative direct reaction in sprue, while the indirect reaction is generally much less pronounced than it is in cases of pernicious anæmia investigated at a corresponding phase of the disease. Thus, in ninety-eight cases of sprue examined soon after admission to hospital, the indirect reaction averaged 0·88 units of bilirubin. Only nine, however, yielded results exceeding 2·0 units (1 mg. per cent.), whereas in pernicious anæmia readings of from two to five units are common.

Other biochemical findings.—Low blood-cholesterol values are common to sprue and pernicious anæmia, but fat-analysis of the fæces, and investigations of the glucose tolerance curve and calcium content of the plasma, may afford information of value in differentiating these diseases. Thus, in a recent series of sixty cases of sprue examined while on a mixed dietary, the average total fat in the dried fæces was 38·5%, and of this 65·3% was split. After 50 grm. of glucose *per os* the blood-sugar curve frequently showed a delayed rise, and often the maximal figure reached did not exceed 30 mg. per cent. Similarly, the total serum calcium tends to be low, and, in our series, the four cases presenting tetany showed readings varying from 5·2 to 6·4 mg.%.

The results which we have reached in an investigation extending over a period

[1] These high protein diets introduced by Fairley (1930) and (1932) are low in fat and carbohydrate and have a ratio of protein : fat : carbohydrate = 1·0 : 0·3 : 1·2. Vide *Trans. Roy. Soc. Trop. Med. and Hyg.*, 131, xxiv, 1930; *Ibid*, 297, xxv, 1932.

of ten years indicate that tropical sprue is essentially a disease of the gastro-intestine, characterized, in its later stages at least, by defective gastric secretion and malabsorption of fat, glucose, and calcium. Dysfunction of the small intestine is the essential lesion, and this is where sprue differs fundamentally from pernicious anæmia.

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Dr. Gordon Goodhart: The part allotted to me in this discussion is the description of a short series of cases of non-tropical megalocytic anæmia with high colour-index, which cannot be classified as pernicious anæmia, and although the title of my contribution has been given as " chronic hæmolytic anæmia," in my view the cases that I have to describe are *not* cases of hæmolytic anæmia. If I were compelled to classify them, I should perhaps place most of them amongst the aplastic anæmias, although, as will be seen from the protocols, they form a very heterogeneous group, with little in common except the blood-picture. They all had certain features in common: all had a very grave anæmia with a high colour-index, all had a very definite megalocytosis and all failed to give the typical response to liver treatment; in saying this it must be remembered that most of them were under observation before the intramuscular preparations now available, and except in the later cases only fresh liver and liver extracts by mouth were given. Two other features were also noticeable. The Price Jones curve, although shifted well to the right, did not show the marked asymmetry that is so usual in true pernicious anæmia, and in some cases it was as symmetrical as the normal curve. I must here add a personal note, since it has been assumed in some quarters that because I have had the advantage of intimate collaboration with Dr. Price Jones for nearly a quarter of a century, and he has always made all my curves for me, therefore, any views I may express may be taken as having his concurrence. This is not so, and although it was Dr. Price Jones who first drew my attention to these symmetrical curves, he does not attach to them the weight that I incline to do, and he considers that I am drawing from a mere visual inspection of the shape of the curve, conclusions which a mathematical calculation would not justify. The other feature to which I wish to draw attention is the absence of the large characteristic polymorphonuclear cells with hypersegmentation of the nuclei that are constantly seen in pernicious anæmia. In all these cases this condition was absent, and in several there was a very definite shift to the left in the Arneth count. In all the cases except one (Case 7) there had been a leucopenia of lymphoid type.

Case 1 (Table I).—P. M., a man, aged 54, was admitted to University College Hospital under the care of Dr. Charles Bolton, and subsequently under Professor T. R. Elliott, suffering from weakness, breathlessness, severe headache and abdominal pain. He was of a lemon yellow tint; the van den Bergh test gave a positive indirect reaction: there was complete achlorhydria and the Wassermann reaction was negative. The fragility of the red cells was normal. There was continuously, and in spite of all treatment, a severe anæmia with a high colour-index. There was no glossitis, but in all other clinical aspects this appeared to be a

typical case of pernicious anæmia, and it was only the failure of response to liver treatment and the symmetrical nature of the Price Jones curve that raised doubt as to the correctness of this diagnosis. Arneth count: shift to left. Fresh liver and liver extracts were given and iron in large doses, but without effect, and blood-transfusions gave only very transient improvement.

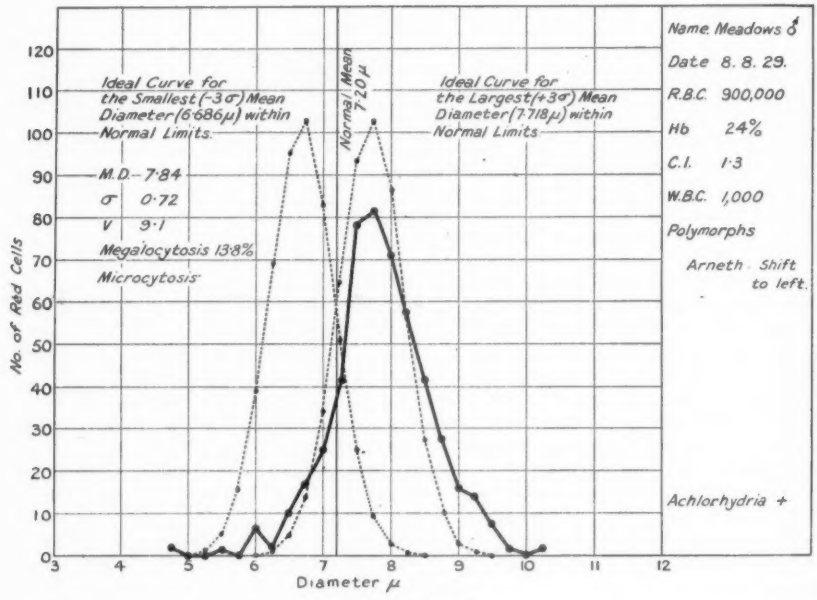

CHART 1.—*Case* 1.

At the autopsy, by Dr. Barnard, the findings were those of an aplastic anæmia. The liver, spleen and kidney all gave a Prussian blue reaction. In describing the marrow, Dr. Barnard reports: "Pink marrow in the bodies of the lumbar vertebræ and red marrow in the sternum which was natural in appearance, with no erosion of the bony trabeculæ. A few scattered patches of red marrow in the neck and throughout all but the lower quarter of the shaft of the right femur. Yellow fatty marrow substance elsewhere. The microscope shows fatty marrow with more white than red cell activity."

TABLE I.

Case 1.

1929	R.B.C.	Hb. per cent.	C.I.	W.B.C.
Aug. 21 ...	1,310,000 ...	30 ...	1·1 ...	1,100
,, 24 ...	900,000 ...	24 ...	1·3 ...	1,000
,, 30 ...	1,300,000 ...	25 ...	0·96 ...	1,500
Sept. 5 ...	1,120,000 ...	25 ...	1·1 ...	1,500
,, 13 ...	1,220,000 ...	24 ...	1·0 ...	440
,, 17 ...	840,000 ...	23 ...	1·3 ...	440
	225 c.c. blood-transfusion.			
,, 19 ...	1,700,000 ...	26 ...	0·8 ...	3,700
Oct. 2 ...	1,160,000 ...	32 ...	1·3 ...	990
,, 16 ...	1,300,000 ...	25 ...	1·0 ...	900
1930.				
Jan. 3 ...	750,000 ...	20 ...	1·3 ...	2,000
Feb. 6 ...	660,000 ...	14 ...	1·08 ...	2,300
,, 15 ...	475,000 ...	12 ...	1·26 ...	1,800

Case 2 (Table II (p. 124).—K. P., a girl, aged 19. Admitted to University College Hospital under the medical unit as an emergency case, suffering from severe abdominal pain and vomiting. She had been in St. George's Hospital for a period of nine months under the care of Dr. E. Bellingham Smith for the same condition, and had only recently discharged herself. In St. George's Hospital she had had an attack of melæna, and during her stay there, had been treated with liver, iron, light, and so forth, but without any obvious improvement. Her condition whilst in University College Hospital was exactly similar to that noted whilst in St. George's. There was a grave anæmia with high colour index, and films showed red cells of obviously greatly increased diameter. She had repeated attacks of the most severe abdominal pain and severe vomiting at regular intervals of from seven to ten days. The van den Bergh reaction was negative; no test meal was possible, but the vomit never contained any free acid and the stools showed no macroscopic evidence of blood. Arneth count: shift to left. After an attack was over the patient recovered quickly and, apart from extreme pallor, was fairly well and very bright; then came another attack, and in twenty-four hours her eyes were sunken,

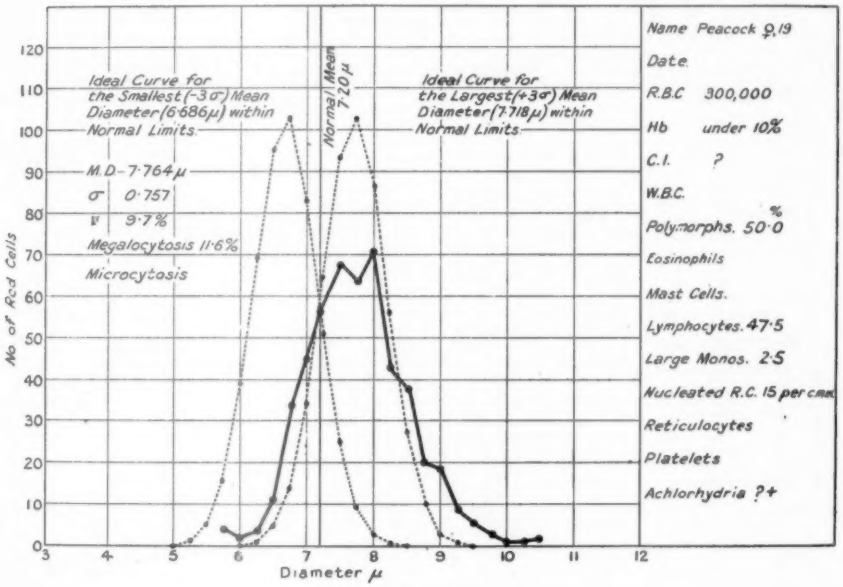

CHART 2.—*Case* 2.

she was collapsed, dehydrated, and almost moribund. Saline and blood-transfusions brought some relief and the attack passed off, only to be renewed a week later. Death occurred following a particularly severe attack.

The possibility of some intermittent obstruction in the small intestine was constantly in mind, but nothing could be detected by palpation, and the patient was never in a condition to justify a laparotomy.

At autopsy, Dr. Barnard found severe inflammation and necrosis of the jejunum, the submucous tissue being much infiltrated and producing polypoid masses in the upper part. There was much blood throughout the small and large intestine. There was free iron in the periphery of the lobules of the liver and in the kidneys, which gave a strong macroscopic Prussian-blue reaction. There were a few small patches of red marrow in the shaft of the right femur and normal red marrow in the bodies of the vertebræ and in the sternum.

TABLE II.

Case 2.

	R.B.C.	Hb. per cent.	C.I.	W.B.C.
Nov. 17 ...	1,120,000 ...	23 ...	1·05 ...	2,200
,, 19 ...	950,000 ...	20 ...	1·0 ...	1,500
,, 30 ...	severe vomiting ...		— ...	—
Dec. 1 ...	1,450,000 ...	30 ...	1·07 ...	18,000
	Intravenous saline and blood-transfusion			
Dec. 8 ...	1,240,000 ...	28 ...	1·0 ...	1,000
,, 13 ...	713,000 ...	15 ...	1·07 ...	2,400
Jan. 1 ...	550,000 ...	10 ...	0·9 ...	1,500
,, 6 ...	770,000 ...	15 ...	1·0 ...	9,000
	(during pain)			
,, 7 ...	Death			

Case 3 (Table III).—O. C., a man, aged 26. He had been a barman for two years and then, in 1928, passed a medical examination for the police force. A fortnight later he had a severe attack of abdominal pain and, later, jaundice. He was then admitted to the West London Hospital, where a laparotomy was performed and the liver found to be about one-third of the normal size. He then had a secondary anæmia with normal blood-fragility and a positive direct van den Bergh reaction. There was ascites, for which the abdomen was tapped twice. After this he improved and returned to his old work for a short time, but a year later (1930) he became ill again and was admitted to University College Hospital under the care of Sir Thomas Lewis.

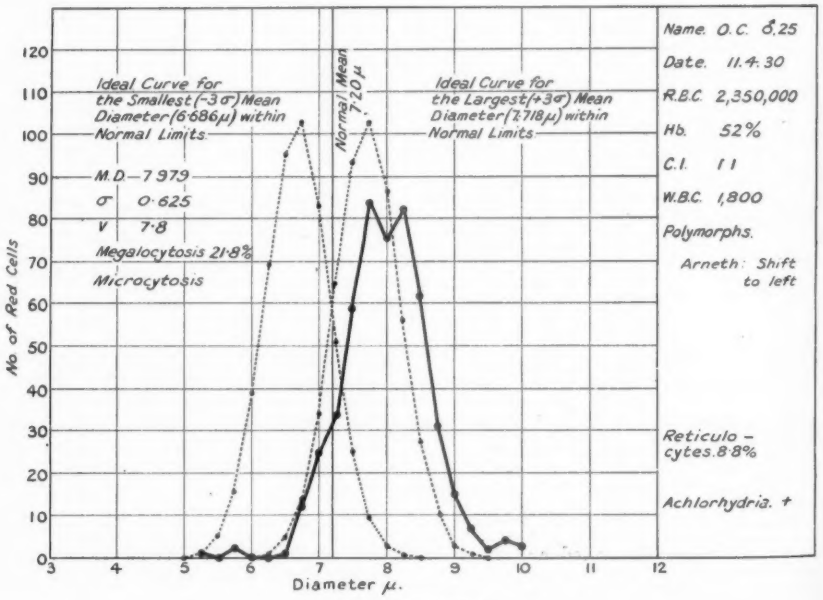

CHART 3.—*Case* 3.

He was pale and breathless, but not obviously jaundiced; there was, however, a weak positive indirect van den Bergh reaction (1 unit). There was a grave anæmia with high-colour index and megalocytosis. Arneth count: shift to left, and there was complete achlorhydria. There was much ascites, for which paracentesis was performed on several occasions, with the removal of many pints of fluid. The liver and spleen were never palpable.

Fresh liver and liver and stomach extracts were given an extensive trial without any beneficial effect, and the patient returned to his home in Ireland.

TABLE III.

Case 3.

1929	R.B.C.	Hb. per cent.	C.I.	W.B.C.
*Mar. 23 ...	4,240,000 ...	61 ...	0·7 ...	8,800
*Apr. 26 ...	3,700,000 ...	53 ...	0·8 ...	3,000
1930.				
Apr. 4 ...	1,900,000 ...	50 ...	1·28 ...	1,500
	Liver treatment.			
,, 11 ...	2,300,000 ...	52 ...	1·1 ...	1,800
,, 15 ...	2,300,000 ...	54 ...	1·15 ...	3,000
,, 17 ...	2,400,000 ...	56 ...	1·15 ...	3,000
,, 28 ...	2,300,000 ...	56 ...	1·19 ...	1,800
May 15 ...	2,100,000 ...	48 ...	1·12 ...	3,000
,, 22 ...	2,100,000 ...	50 ...	1·19 ...	3,000

* For these two counts I am indebted to the Registrar of the West London Hospital.

Case 4 (Table IV, p. 126).—C. H., a woman, aged 27. First came under observation by Dr. McNee for treatment for lymphadenoma by deep X-ray therapy in March, 1930. The clinical diagnosis was supported by biopsy. At that time there was a mild secondary anæmia. She was spending much of her time on the East Coast and only came up intermittently for blood-counts. She was admitted to University College Hospital under the care of Dr. McNee in August, 1930. By the middle of September it was apparent that a striking alteration had taken place in the blood, for in addition to the anæmia there was now an obvious megalocytosis. The Arneth count showed a shift to the left. This I regarded as an X-ray

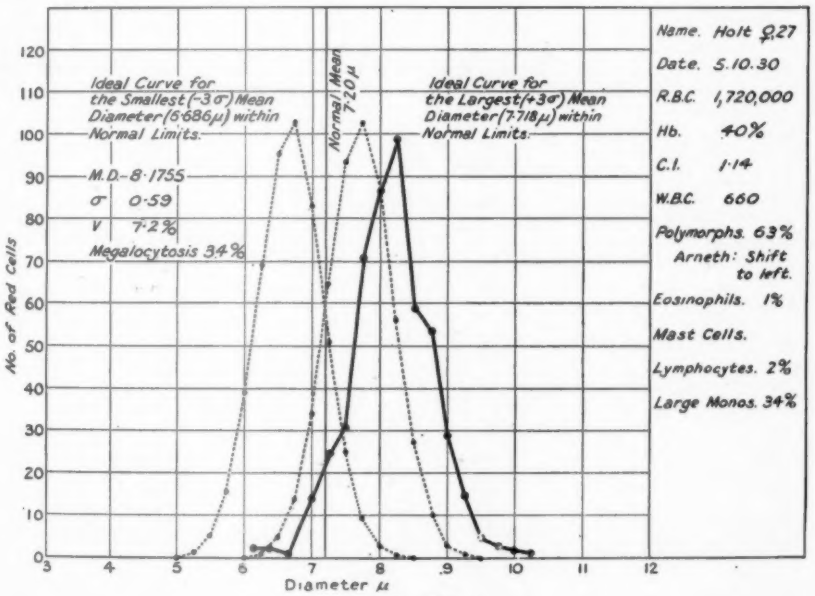

CHART 4.—*Case* 4.

aplasia, but in view of the cases of lymphadenoma associated with megalocytosis, reported by Professor Stanley Davidson, there may probably be some other explanation. So far as could be judged clinically, there was much improvement with regard to the lymphadenoma, for glands and spleen decreased in size very considerably, but the anæmia resisted all methods of treatment in which liver therapy had a prominent place. Iron in large doses seemed, at one time, to promise a favourable response, but it was borne badly by the patient and continuous dosage could not be maintained. She suffered from several severe febrile attacks, including a very severe influenza, and died fifteen months after first coming under observation. Permission for post-mortem examination could not be obtained.

TABLE IV.

Case 4.

1929	R.B.C.	Hb. per cent.	C.I.	W.B.C.
Mar. 27	4,200,000	78	0·92	4,200
	Deep X-ray therapy.			
June 24	4,000,000	70	0·87	3,600
Aug. 26	2,700,000	48	0·8	2,000
Sept. 17	2,700,000	44	0·8	—
,, 29	1,890,000	40	1·17	1,800
Oct. 11	Blood-transfusion.			
,, 15	2,560,000	40	0·80	1,600
,, 16	Blood-transfusion.			
,, 18	3,540,000	68	0·9	600
Dec. 13	1,580,000	35	1·1	900
,, 31	990,000	18	0·9	700
	Blood-transfusion.			
1931				
Feb. 15	680,000	22	1·5	1,100
Mar. 4	1,140,000	21	0·9	4,300
	Ferri et ammon. citr. gr. xxx, t.d.s.			
,, 20	1,480,000	33	1·12	3,100
Apr. 2	1,860,000	46	1·24	1,100
,, 9	Iron discontinued.			
,, 14	2,610,000	46	0·88	1,100
June 2	1,820,000	36	1·0	1,100
,, 11	1,800,000	23	0·68	1,000

Case 5 (Table V).—A. A., a woman, aged 54, was admitted to University College Hospital in September, 1931, under the care of Dr. Bolton, suffering from severe anæmia, bleeding from the rectum and vagina, epistaxis and purpura. She had been ill with these symptoms in varied degree for a year. The liver and spleen were not palpable. The van den Bergh

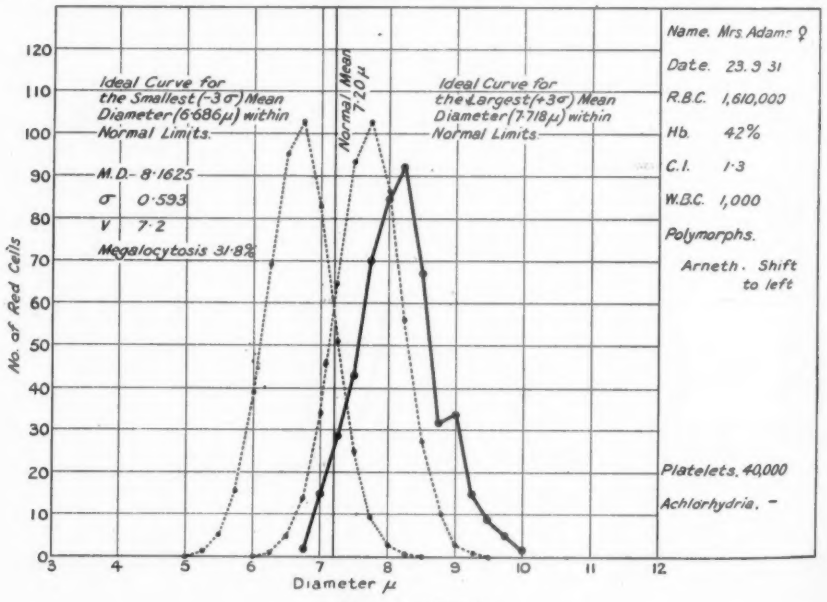

CHART 5.—*Case 5.*

reaction was negative and the gastric contents contained free hydrochloric acid. The anæmia was of megalocytic type with high colour-index, but the platelet count was only 40,000 per c.mm. Arneth count: shift to left. Liver, half a pound daily, had no effect, and in view of the low platelet count after a series of transfusions, the spleen was removed. This was followed by a temporary cessation of the hæmorrhage and a rise in the platelet count. The uterine

hæmorrhage, however, returned very soon and she was transferred to the gynæcological wards for radium treatment in November.

In March, 1932, she was re-admitted with epistaxis and again, severe anæmia. She had been treated with one and a half pounds of liver and 90 gr. pil. ferri daily, and more recently she has had intramuscular injection of campolin, but there has been no response.

TABLE IV.

Case 5.

1931	R.B.C.	Hb. per cent.	C.I.	W.B.C.	Platelets
Sept. 23	1,640,000	42	1·3	1,000	40,000
Oct. 3	Splenectomy				
,, 8	2,300,000	40	0·8	4,500	400,000
,, 21	1,480,000	28	1·0	3,500	—
Nov. 5	2,000,000	44	1·1	4,000	200,000
,, 17	3,400,000	52	1·09	—	400,000
	Radium therapy				
1932.					
Mar. 9	½ lb. liver and gr. 90 pil. ferri daily				
,, 11	1,160,000	26	1·18	—	—
,, 17	1,100,000	27	1·12	—	—
,, 28	850,000	27	1·58	1,300	—
	No reticulocyte response.				

Case 6.—E. P., a woman, aged 24, was admitted to University College Hospital under the care of Dr. Charles Bolton, suffering from abdominal pain and diarrhœa. She had a severe anæmia of megalocytic type: R.B.C. 1,600,000 per c.mm., Hb. 50%, C.I. 1·5, W.B.C. 3,500.

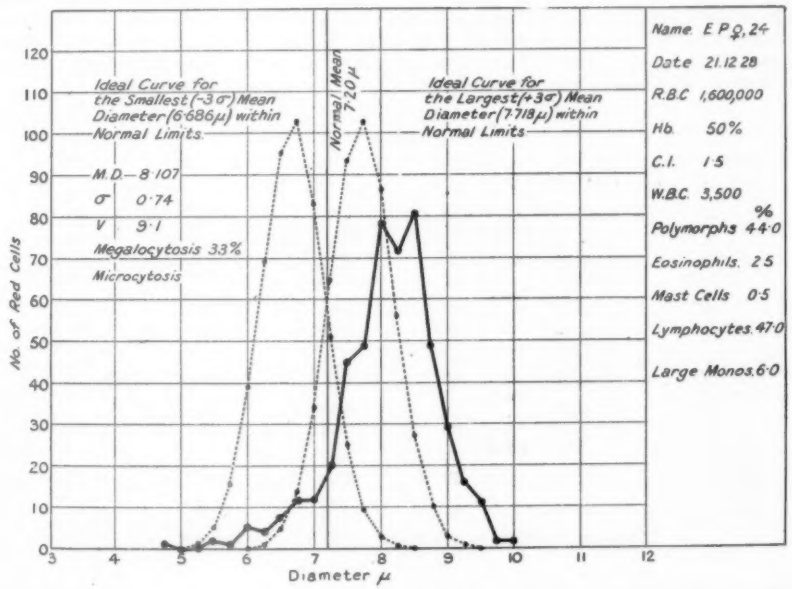

CHART 6.—*Case* 6.

She was very difficult to treat and made a fuss about taking liver in any form, though in the end she took a fair quantity, but without any reticulocyte or red-cell response. She was transferred to Mr. E. K. Martin for laparotomy, and he found tuberculous stricture of the small intestine. Numerous counts were made, but little variation was found.

Case 7.—Mrs. E., aged 52, was admitted to the Fulham Hospital in January, 1930, on account of hæmoptysis and anæmia. The skin was of a slightly lemon-yellow tint and the patient's appearance, clinically, was like that in pernicious anæmia. She had had one large hæmorrhage thought to have come from the lung. A blood-count was made showing R.B.C. 1,950,000 per c.mm., Hb. 54%, C.I. 1·4, W.B.C. 10,000; nucleated red-cells 400 per c.mm. The leucocytosis (polymorphonuclear 77%), and the nucleated red-cells suggested some other cause for a megalocytic anæmia than a true Addisonian anæmia, and an X-ray examination revealed an obvious thoracic lesion. The patient died before a complete examination could be made, and at the post-mortem examination a large tuberculous cavity was found in the right lung, with extensive caseating bronchopneumonia. There was no free iron in the liver or kidneys. The bone-marrow was fatty and showed very slight activity.

In this case although the condition was clearly not one of pernicious anæmia, the Price Jones curve shows the typical asymmetry associated with that condition.

Case 8 (Table VI).—A man, aged 22, was admitted to University College Hospital under the care of Professor T. R. Elliott, in October, 1926, suffering from diarrhœa and secondary anæmia. He did well and was discharged without any apprehension of future trouble. In February, 1928, he was re-admitted with slight jaundice, fever, and wasting. He was then found to have a megalocytic anæmia, complete achlorhydria, and a positive indirect van den Bergh reaction.

The red cells at that time were 2,400,000 per c.mm., Hb. 68%, C.I. 1·4, W.B.C. 2,800. He was treated with liver extract followed by whole liver. The reticulocyte response was poor and there was none of the general clinical improvement and feeling of well-being that is characteristic of the liver response in pernicious anæmia, but the blood improved steadily and in five weeks' time the count was R.B.C. 4,000,000, Hb. 80%, C.I. 1·0, W.B.C. 5,400. He left off taking liver and was re-admitted to hospital a fortnight later very ill and deeply jaundiced, with enlargement of liver and spleen. A laparotomy was performed with a view to splenectomy, but nodules of growth were found in liver, spleen, and mesenteric glands and proved to be lymphosarcoma. Death occurred at home from septicæmia and no post-mortem examination was made.

TABLE VI.

Case 8.

1926	R.B.C.	Hb. per cent.	C.I.	W.B.C.	Ret.
Oct. 7	3,350,000	54	0·8	8,000	—
1928					
*Feb. 10	2,400,000	68	1·4	2,800	2·6
	Liver extract = 710 grm. liver				
,, 16	2,440,000	66	1·28	3,700	2·6
,, 17	2,280,000	64	1·45	—	5·4
,, 19	2,700,000	66	1·22	2,800	5·7
,, 20	Whole liver				
,, 21	2,700,000	66	1·22	1,300	5·8
Mar. 1	2,920,000	64	1·10	3,300	7·8
,, 6	3,160,000	70	1·12	3,100	8·2
,, 10	3,200,000	70	1·12	5,100	3·0
,, 14	4,000,000	80	1·0	1,200	3·6
May 5	Off liver				
,, 12	4,640,000	78	0·84	5,300	—
,, 31	3,870,000	60	0·77	4,400	—
June 16	Splenectomy				
1929.					
Nov. 29	4,080,000	78	0·97	9,100	—
1930.					
Mar. 26	5,100,000	86	0·87	4,200	—

* The detailed counts in this case I owe to Dr. Janet Vaughan.

Dr. Lucy Wills: "Tropical macrocytic anæmia" [1] is a severe anæmia, especially common in pregnant women. It is quite distinct from the so-called "pernicious anæmia of pregnancy" occurring in temperate countries. As I have only studied this condition in India, and among women—the majority pregnant—this paper will, in the main, deal with such cases, and to simplify the issue further, will refer only to uncomplicated ones.

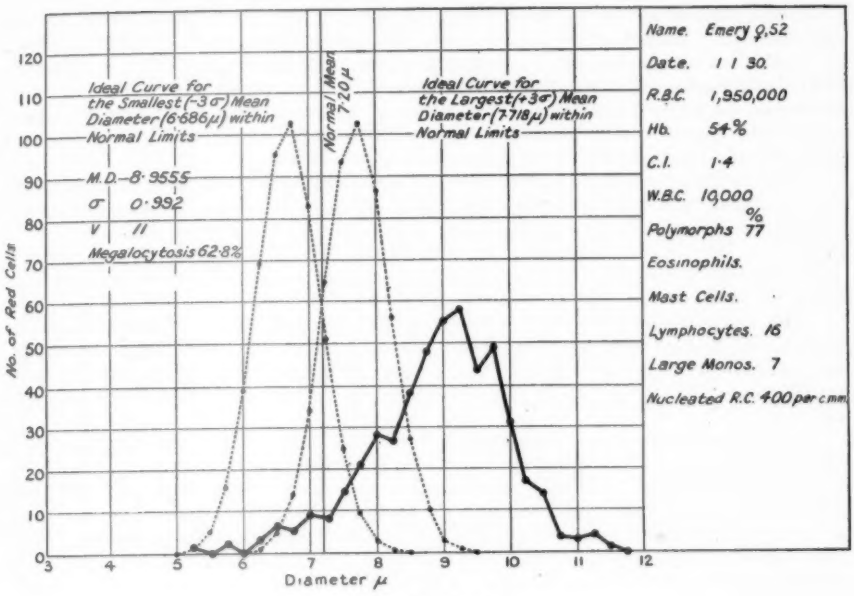

CHART 7.—*Case* 7.

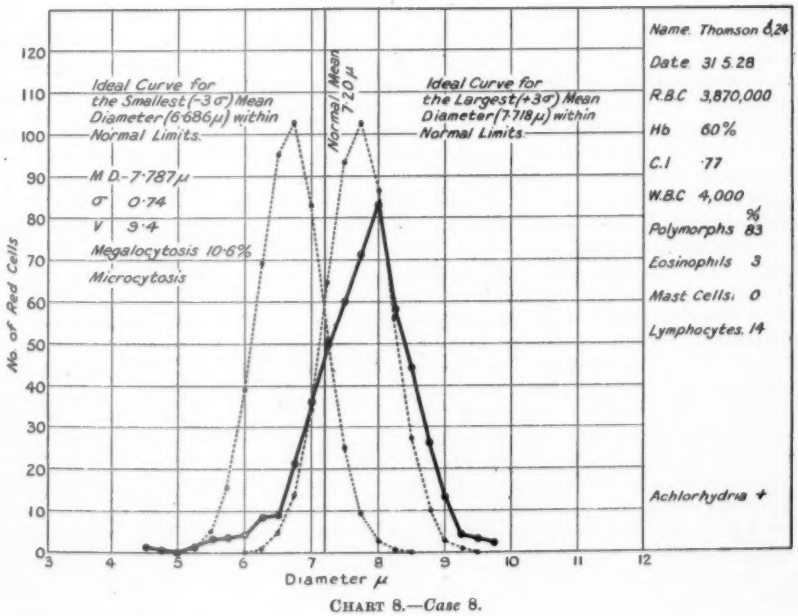

CHART 8.—*Case* 8.

The condition is reported from many tropical countries, especially India [2] [3] [4], China [5] and West Africa [6]. In India it is more common in the southern half, where it occurs among all communities and in all grades of society. If it is a nutritional disease this may seem strange, but customs and religion limit the diet of all classes, and purified foods are increasingly common. Rice forms an important part of the diet of a large proportion of the patients. The disease is seasonal, the majority of the cases occurring between October and April.

It is difficult to form an opinion as to its duration, as patients seldom come up for treatment before the anæmia has become extreme, and histories are completely unreliable. The final breakdown may, however, be very rapid. I have seen a case in which the red-cell count fell one and half million in ten days. Patients most frequently report in the latter half of pregnancy, but I have had severe and fatal cases as early as the fourth month.

The usual course is for the patient to be admitted in the seventh or eighth month and to have a premature labour, followed either by rapid improvement, or, frequently, by collapse and death. Some cases, however, only develop after delivery, sometimes several weeks later. In the non-pregnant cases the disease is far more chronic.

The symptoms, other than those directly referable to the anæmia, are very variable. Balfour [2], quoted by Witts [7], describes fever, diarrhœa, and vomiting as marked symptoms. Fever is common, but in a land where there may be "hot fever" and "cold fever" and either may be associated with a normal temperature, a history of "fever" means nothing. In the later stages when the patient is under observation, most cases have some rise of temperature—in certain cases marked, and suggestive of typhoid or septicæmia. A careful examination of the blood (cultures, Widal tests, etc.) stools and urine, excluded these conditions in our cases. Diarrhœa and vomiting are not typical. During my first two winters there was hardly a case with such symptoms, though during the two previous seasons they had been so common that Dr. Balfour, who was then working on the disease, described diarrhœa and vomiting as marked symptoms. The occurrence or absence of these symptoms is probably related to the incidence of diarrhœa in the general population. Sore tongue and mouth are more constantly present. The spleen is frequently enlarged and sometimes tender. Nerve changes are absent.

The anæmia is severe. In 54 consecutive cases 32 had initial red-cell counts below a million. The death-rate, before the discovery of liver therapy, was high (42% in Balfour's series) and fell only to 33% in a series that were treated with liver extract, as so many patients were moribund when admitted and died within a few hours undelivered, or went immediately into labour and died within forty-eight hours, before liver therapy could help them. After I discovered the use of marmite (yeast extract) the death-rate fell considerably, but the series so treated was small, and moreover publicity was better, so that cases were reporting earlier.

The blood-picture is that of a macrocytic anæmia with both normoblasts and megaloblasts present, the former being more frequent than in idiopathic pernicious anæmia. The Price Jones curves show a shift to the right and a marked increase in variability. There is little poikilocytosis. There is no increase in the serum bilirubin. The white-cell counts are variable in the pregnant cases, but in the non-pregnant there is commonly a leucopenia. The test meal shows the presence of free acid in normal amounts in the majority of cases. The average serum calcium is 9·0 mg. per 100 c.c., i.e., within normal limits. There is a moderate increase in the non-protein nitrogen and in the urea of the blood in those cases with red-cell counts below a million. As I have mentioned before, I could find no evidence of a constant infection. Balfour reports areas of hyperplasia alternating with aplastic areas in the bone-marrow from two cases. I was unable to obtain permission for post-mortem examinations.

The result of treatment of this anæmia was invariably poor before the advent of liver therapy; all remedies, including iron—and, according to the Calcutta School, blood-transfusions—were useless. Now, uncomplicated cases can be successfully treated, not only with liver extract but also with marmite. The result of such treatment is shown in Charts 1, 2, 3 and 4. There was no control period, but this was unavoidable. The non-pregnant patients had been in hospital for some time, receiving general treatment, and were desperately ill before they came under our care. Bitter experience had taught us that urgent treatment was necessary to save the pregnant cases. It is important to give large doses of liver

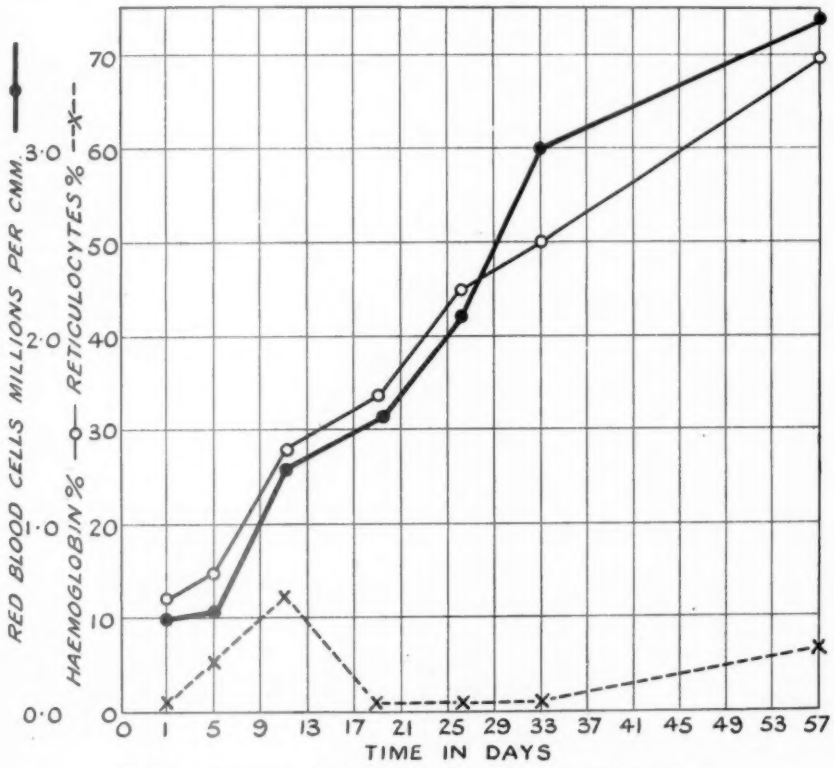

CHART 1.—Response to treatment with liver extract. Non-pregnant case.

extract, the equivalent of 600 grm. of fresh liver, as the response to smaller doses is slow, and time is all important.

A teaspoonful of marmite, three or four times a day, or twice a day in the non-pregnant cases, is found to cause a rapid improvement, with a maximal reticulocyte response, generally on the fifth day of treatment. It has been suggested by Davidson [8] that the action of marmite is due to its vitamin B content toning up the intestinal tract and leading to better digestion and assimilation, aided by a better diet in hospital. I cannot agree with this suggestion. The majority of the patients have all their food and frequently their water sent in, and in fact the first patients in whose cases marmite was tried were poor, but strict, Brahmins, every

particle of whose food was sent in from their homes. As regards the tonic action of marmite, the rapidity with which it acts (maximal reticulocyte response in five days) suggests a specific effect, more especially as some of these patients were taking absurdly little nourishment at the time, owing to a prejudice against food during an illness.

This anæmia has been classified as a nutritional anæmia, and it is interesting to review the evidence in support of this classification. The world distribution in areas where deficiency diseases are frequent, suggests a nutritional origin: this is supported by the dietetic survey which Dr. Talpade and I [9] made in Bombay, showing the

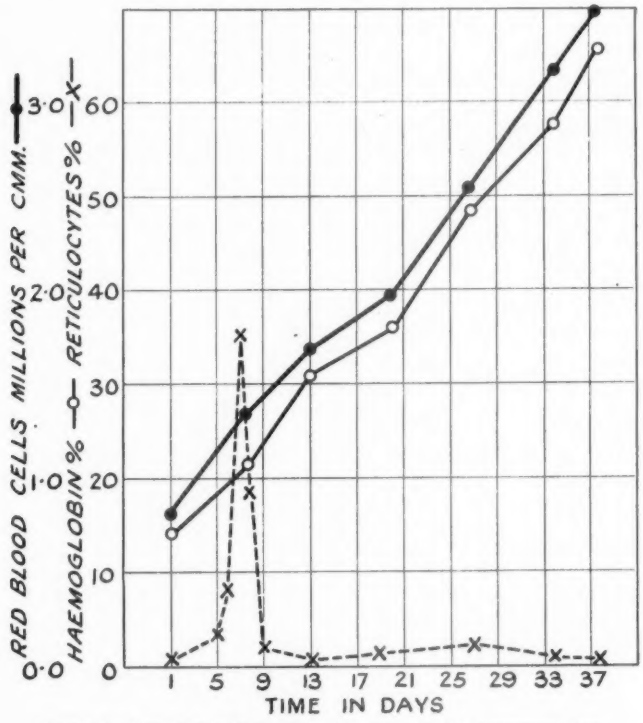

CHART 2.—Response to treatment with marmite. Non-pregnant case.

gross deficiencies in the diet of all the hospital classes. The association of the condition with pregnancy or lactation, when extra demands are made on the maternal organism, and the improvement so commonly seen after delivery, are characteristics shared by other deficiency diseases such as osteomalacia and beri beri. The failure, after an exhaustive search, to find any evidence of an infective agent, negatives an infective origin. The absence of any evidence of faulty digestion or absorption in many cases would suggest that the deficiency is in some extrinsic factor in the diet rather than in any intrinsic factor. As a result of the dietetic survey made in Bombay and of rat experiments carried out at Coonoor [10], I originally formed the opinion that this extrinsic factor was probably related to vitamins A and C, but

monkey experiments demonstrated that this was not so. In these experiments Dr. Billimoria and I were able to produce a macrocytic anæmia associated with megaloblastic hyperplasia of the bone-marrow in monkeys fed on a diet in common use among sufferers from anæmia in Bombay. This diet was deficient in all the vitamins (vitamin D was supplied by sunlight), in protein, and in salts. Without any additional rations, all the animals fed on it failed to grow, became anæmic and died. With the addition of extra rations of vitamins A and C and a limited quantity of milk, the animals grew well but became anæmic. As growth was good, it is, I think, fair to assume that not only were vitamins A and C present in adequate amounts, but

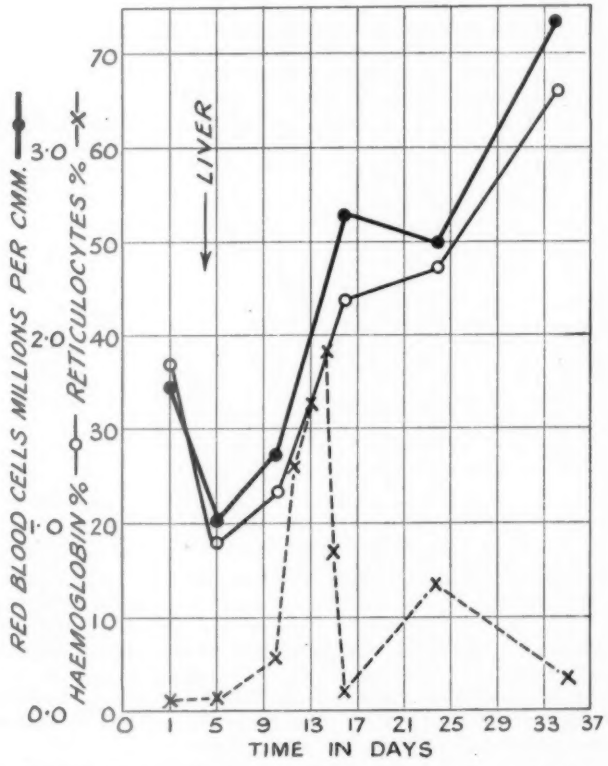

CHART 3.—Response to treatment with liver extract. Pregnant case.

vitamin B_1 was present also in this augmented diet, and that these factors were not those producing the anæmia. That the factor is related to the vitamin B complex is suggested by the fact that another animal which received, besides the extra rations mentioned above, an additional yeast ration, remained in perfect health throughout the experimental period. Further, this monkey anæmia responded well to marmite, a fact which led to the trial of this remedy in cases of tropical macrocytic anæmia. Marmite is a good source of vitamin B_2 as well as of vitamin B_1, so that the question of the possible ætiological importance of the former must be considered. Sure and

co-workers [11] have shown that a certain percentage of rats on a B_2 deficient diet became anæmic, but Guha and Mapson [12] suggest that the anti-anæmic factor is not vitamin B_2 itself, but is some associated factor. That this extrinsic factor is not Cohn's anti-anæmia factor, present in liver extract, is clear from the fact that although both marmite and liver extract are active in the treatment of tropical macrocytic anæmia, marmite is inactive in the treatment of Addisonian pernicious

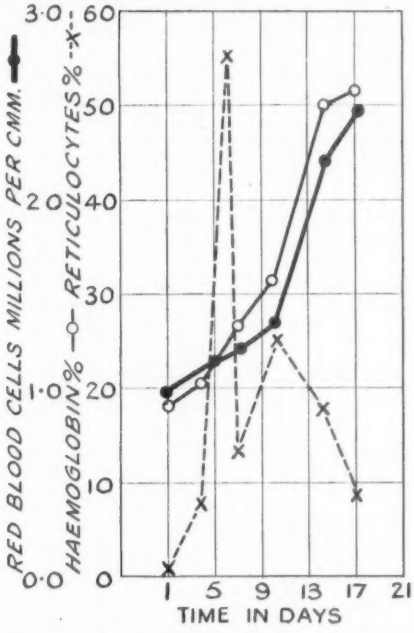

CHART 4.—Response to treatment with marmite. Pregnant case.

anæmia (Davidson [8], and Wills [unpublished]). Both marmite and liver extract are, however, good sources of the vitamin B complex, and one is tempted to ascribe their curative action in tropical macrocytic anæmia to some part of this complex other than vitamin B_1, but till further work has led to the isolation of the active fraction the exact nature of this factor must remain in doubt.

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Dr. Price Jones: The common feature of every sample of blood-cells in health and disease is "anisocytosis" or inequality of size. The chief use of "distribution curves" is to express this anisocytosis, or the variability of the diameter of the cells. From the distribution the mean diameter is calculated and the position of the curve and mean diameter is shown in relation to the normal curve and mean diameter which I have derived from the measurement of 50,000 healthy red cells. This position enables us to say if the distribution is megalocytic, microcytic, or both, or neither. By enumerating the cells distributed outside the limits of the normal distribution, it is possible to estimate the degree of megalocytosis or microcytosis as the case may be. The curve also shows if the distribution is symmetrical or skew. In anæmia there is no correlation between the mean diameter and the degree of anæmia. There is, however, a direct correlation of the anisocytosis or variability and the severity of the anæmia. I suggest that in conditions associated with marrow dysfunction the curve is shifted to right or left and the distribution has high variability and is more or less asymmetrical or skew. In those conditions in which the cells are acted on by some common factor in the circulation, and only indirectly or secondarily associated with disordered hæmopoiesis, the variability is more frequently normal or relatively slight, and the distribution is more or less symmetrical.

Professor M. J. Stewart (Leeds) referred to a number of cases of trinitrotoluene poisoning which he had seen during the war (*Proc. Roy. Soc. Med.*, 1917, x, 10, in which there were notable blood changes, usually of aplastic type. In three cases, however, there was a definitely megalocytic anæmia, and in one case, that of a girl, aged 18, showers of megaloblasts appeared in the circulating blood. The red cells in this case fell to below a million and the colour-index was 1·5 to 1·8. Ultimately the patient made a good recovery, both from the anæmia and the liver necrosis. Dr. Goodhart's case of megalocytic anæmia with contracted liver might be an example of chronic liver atrophy (post-necrotic fibrosis). Had any of the speakers investigated the blood in acute, subacute, or chronic atrophy (cytolytic necrosis) of the liver?

Dr. Reginald Lightwood, speaking with regard to the occurrence of megalocytic anæmia in childhood, said that pernicious anæmia, as seen in adults, was almost unknown in young children. In part explanation of this fact it was conceivable that in them the stomach was more effective in producing Castle's intrinsic factor, though, by analogy, this was unlikely, on account of the frequency of hypochlorhydria in children.

In so far as some cases of megalocytic anæmia depended on faulty intestinal absorption, cœliac disease might be expected to produce megalocytic anæmia, and among thirty-nine cases of cœliac disease (Fanconi), three had been quoted as showing the megalocytic blood picture. More usual in this disease was an iron-deficiency anæmia with low colour-index. A persisting relative lymphocytosis might be another characteristic of the blood picture.

The infrequency of megalocytosis in children might also be attributable to a difference in the bone-marrow, which was known to be relatively more active throughout childhood.

Dr. Janet Vaughan said that in investigating a series of thirteen cases of cœliac disease or idiopathic steatorrhea in adults, she had found two with a megaloytic hyperchromic anæmia. In view of the observations of Dr. Lucy Wills on the treatment of tropical anæmia, both patients had been given large daily doses

of marmite. In both there had been prompt improvement, the reticulocytes reaching the maximum level calculated from the initial red-cell count. The return to a normal blood-picture had been associated with a notable gain in weight, as in Addisonian pernicious anæmia. Other symptoms, e.g., diarrhœa and tetany had been unaffected. She presumed, therefore, that marmite exerted a direct effect upon disordered hæmopoiesis.